THE STUDENT'S HANDBOOK OF PHYSIOLOGY

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BY THE LATE

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PUBLISHERS' PREFACE.

THIS book was begun by the late Dr ARTHUR CLARKSON, a distinguished physiologist and teacher, and the author of a well known Atlas and Text-Book on Histology.

After his untimely death, Dr DAVID FARQUHARSON, Professor of Physiology in St Mungo's College, Glasgow, undertook to complete the work by writing some of the Sections on the Special Senses and the Chapter on the Central Nervous System. With these exceptions the work is that of the late Dr Clarkson.

A large number of the Illustrations are new, from drawings by Dr Clarkson and Dr Farquharson, who is responsible for the majority of those in the portion of the work which he has written. To these have been added by purchase many of the latest figures from leading British and Continental authorities. For courtesy in supplying the necessary clichés, our thanks are cordially extended to Messrs Wright & Co., Bristol (the publishers of Dr Clarkson's "Text-Book on Histology"); Bailliere, Tindall & Cox, London; Cassell & Co., London; Winter & Co., Heidelberg; Fischer, Jena; Hirzel, Leipzig; Masson & Co., Paris; Vieweg & Son, Brannsweig; and Doin, Paris, as well as to others who have kindly granted their consent to the reproduction of drawings.

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HANDBOOK

OF

PHYSIOLOGY.

CHAPTER I.

BIOLOGY is the science of life in the widest sense of the word; Physiology is the science of the phenomena of living matter in a more limited one, and deals more especially with its functions. It may be considered to rest on a basis of other sciences, including Anatomy, Chemistry and Physics, and is concerned with the structure, chemical composition and functions of the organism (or its smallest part), whether animal or vegetable. In the following pages Animal Physiology only is dealt with.

The science is thus not a simple but a compound one, capable of being resolved into subdivisions, which are widely distinct from each other in the nature of the phenomena with which they deal. Yet, as they are to a great extent interdependent, *i.e.*, the one being of advantage in the understanding of the others, it has for long been customary to interweave them under the common generic name, and to treat them as forming constituent parts of one and the same great subject. It will be at once apparent that our knowledge of function would be necessarily incomplete were it not subtended by an acquaintance with the arrangement of the parts of the organism (anatomy), with its minute structure (histology), and with its chemical composition (chemical physiology).

THE CHEMICAL CONSTITUENTS OF THE BODY.

I. Inorganic.—These consist of water and salts. Water is present to the extent of 60 per cent. of the body weight. Of the salts, $NaCl$ is found the most widely distributed; it especially facilitates osmosis and serves to hold the globulins in solution. Calcium phosphate and calcium carbonate form the greater part

by weight of the bones. Sodium phosphate and potassium phosphate occur in most of the fluids of the body ; the acid reaction of the urine being due to the presence of acid sodium phosphate. Sodium carbonate and acid sodium carbonate (bicarbonate) occur in the blood in the plasma, whilst iron forms an important constituent of the hæmoglobin in the coloured corpuscles. Potassium chloride is found in the body generally, but especially in muscle and the red blood corpuscles. Free hydrochloric acid occurs in the gastric juice.

II. Organic.—These are by far the more interesting, physiologically, and are represented by three great groups—Proteids, Carbohydrates and Fats.

I.—THE PROTEIDS.

Proteids are the most important class of food materials, as they alone contain many of the essential elements, such as nitrogen, phosphorus, sulphur, &c., required both for the construction and the repair of protoplasm. The native proteids are all very complex bodies, *e.g.*, egg-albumin has the following formula :—

$$C_{204}\ H_{322}\ N_{52}\ O_{66}\ S_{2}.$$

They are all composed of the following elements, viz., C H O N and S.

The percentage of the constituents varies, however, to a certain extent—

From......	C. 51·5 ;	H. 6·9 ;	N. 15·2 ;	O. 20·9 ;	S. ·3.
To	54·5 ;	7·3 ;	17 ;	23·5 ;	2·0.

(*Hoppe-Seyler*).

It will therefore be apparent that carbon forms practically one half of the molecula, nitrogen one-sixth, and sulphur one-hundredth. The percentage of nitrogen is of peculiar importance, as it enables us to ascertain, through an estimation of the amount of nitrogen eliminated, the extent of the proteid break-down in the body. (Thus the excretion of ten grammes of nitrogen by an animal shows us that a little over sixty grammes of proteid must have been broken down in metabolism).

Proteids are found in practically all the tissues and fluids of the body. Some are soluble in distilled water, whilst others are not. They are all colloidal, though many can be crystallised, while they are generally coagulable by heat, mineral acids and alcohol. They are the most important chemical elements in muscular, glandular and nervous tissue, and also occur in large

amount in the blood and the lymph. On the other hand, they are practically absent in urine, bile, sweat, and tears, though in pathological conditions, such as inflammatory diseases of the kidney, they may be present to a very considerable extent.

All the proteids are lævo-rotatory, *i.e.*, they rotate the ray of polarised light to the left. The amount of the rotation varies with the different members of the group :—

Serum-albumin = 56°,
Egg-albumin... = 35·5°.

They all give certain colour and precipitation tests, which are of very great importance.

Group or class tests for proteids.—1. *Xanthoproteic test.*—On the addition of a little nitric acid to a solution containing proteid, a yellow colouration or precipitation forms as the fluid is boiled. If the solution be then cooled and a little ammonia or caustic alkali added, the colour changes to a very characteristic orange tint.

2. *Piotrowski's test.*—The addition of a small quantity of a weak solution of cupric sulphate, and excess of caustic hydrate to a solution of ordinary proteid gives a distinct violet colouration; with peptone the reagents give a pink reaction unless an excess of copper be present, when the ordinary violet colouration may appear.

3. *Millon's test.*—This test is not obtained from those proteids which do not contain aromatic compounds—such as tyrosin—in their composition. The reagent (acid nitrate of mercury) gives a white precipitate with proteid or solution, which becomes red on boiling.

4. *Adamkiewicz's test.*—A considerable excess of glacial acetic acid is added to the solution, which is then boiled. On cooling, a little strong sulphuric acid is slowly added, when a violet colour appears at the line of junction. The reaction has been shown by Hopkins and Cole to be due to the presence of glyoxylic acid in the acetic acid.

5. *Hopkin's modification* of this test is very commonly employed. An equal part of dilute glyoxylic acid is added to the solution and then some strong sulphuric acid, when it acquires a rich violet colour.

ANALYSIS OF PROTEID.

Several methods have been devised by which the complex proteid molecule has been split up into simpler and apparently essential cell groups. Of these methods we will only mention a few :—

1. The prolonged action of heat on proteid in the presence of an alkali, such as baryta.

2. Destructive distillation with acids, such as hydrochloric acid, a little stannous chloride being added to the mixture to prevent oxidative changes.

3. Prolonged digestion with trypsin—the active proteolytic ferment of the pancreatic juice.

A large number of more or less simple bodies are obtained belonging to the following groups :—

1. The amino acids, such as (1) mono-amino acids, as aspartic acid, leucin and glycin; (2) di-amino acids, as arginin, lysin and histidin (histones); (3) aromatic mono-amines, as tyrosin; (4) sulphur-containing amine, as cystin.
2. Purin bases.
3. Chromatic bodies, such as indol.
4. Ammonia.
5. A carbohydrate radicle.

Of these, the amino acids are in many respects the most interesting. They can be formed from any of the monobasic fatty acids ($C_nH_{2n}O_2$), such as acetic, propionic, butyric or caproic, by the substitution of amidogen (NH_2) for one of the atoms of hydrogen.

Thus from

Acetic acid, CH_3COOH, we get Glycocoll or Glycin, CH_2NH_2COOH.
Caproic acid, $C_5H_{11}COOH$, we get Leucin, $C_5H_{10}NH^2COOH$.

Similarly, aspartic acid is the amine of succinic acid, and glutamic acid that of pyrotartaric acid.

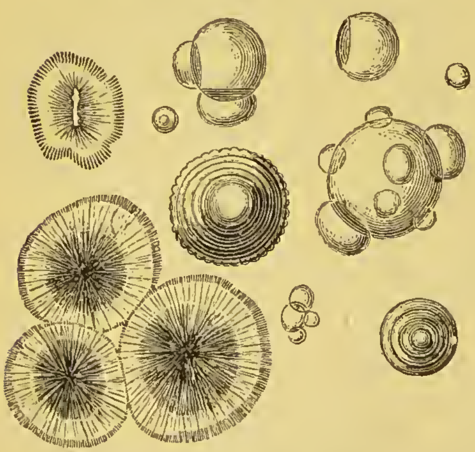

Fig. 1.—Leucin Crystals.

Both leucin and tyrosin can be obtained readily by making a pancreatic digest of proteid for twenty-four hours, and later evaporating it down, when bundles of tyrosin crystals are deposited. The mother liquid also contains leucin, which can be obtained by further evaporation and extraction with alcohol.

Tyrosin cannot be included, however, in this group of simple amino fatty acids, as it contains also an aromatic element, one of the H atoms being replaced by p. oxyphenol (C_6H_4OH) thus :—

Propionic acid...Amino-propionic acid.....p. Oxyphenol-amino propionic acid.
(C_2H_5 COOH)...C_2H_4 ; NH_2 ; COOH..... C_2H_3 ; NH_2 ; C_6H_4OH ; COOH.

The hexones are also a very important constituent of proteid,

Fig. 2.—Crystals of Nitrate of Urea.

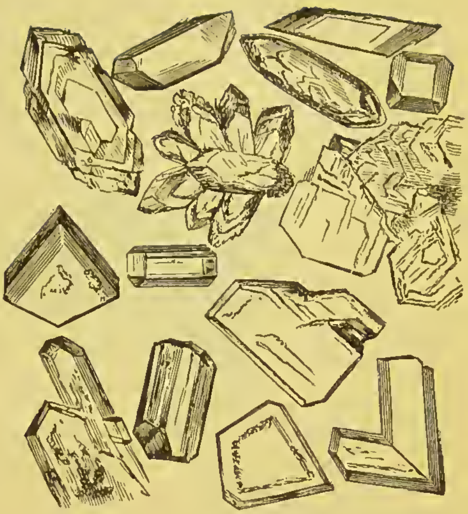

Fig. 3.—Crystals of Oxalate of Urea.

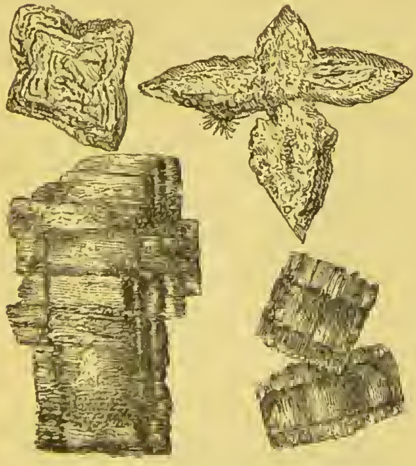

Fig. 4.—Crystals of Uric Acid Rapidly Separated.

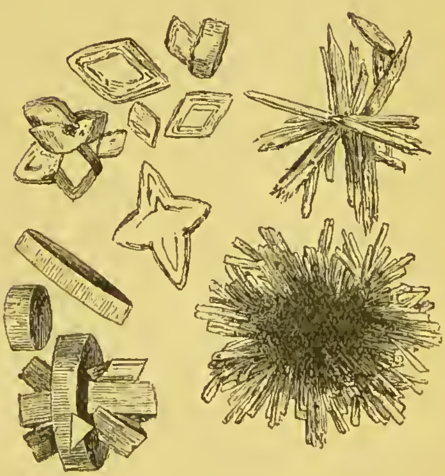

Fig. 5.—Crystals of Uric Acid Slowly Separated.

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for, they are always obtained on its disintegration, and the simplest types of proteid (the protamins) seem to be composed almost entirely of these elements.

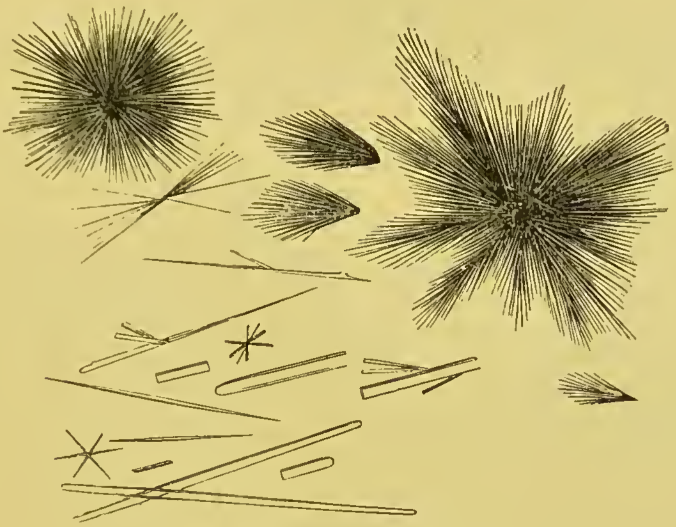

Fig. 6.—TYROSIN CRYSTALS.

Thus Kossel has shown that sturin, the protamin in the spermatozoa of the sturgeon, breaks up into three molecules of histidin, arginin and lysin.

$$C_{36}H_{69}N_{19}O_7 + 5H_2O = \underset{\text{(Histidin)}}{C_6H_9N_3O_2} + \underset{\text{(Arginin)}}{3C_6H_{14}N_4O_2} + C_6H_{14}N_2O_2 \text{ (Lysin)}.$$

The di-amino acids are commonly called the hexones, as they all contain six atoms of carbon. (Lysin $C_6H_{14}N_2O_2$—Arginin $C_6H_{14}N_4O_2$—Histidin $C_6H_9N_3O_2$).

Arginin is found largely in certain seeds and plants; it is very readily broken down on boiling with baryta into urea.

CLASSIFICATION OF PROTEIDS.

1. Simple or Native proteids;

Albumins, *e.g.*, egg- or serum-albumin.
Globulins, *e.g.*, serum-globulin, fibrinogen, crystallin.

2. Modified proteids;

(1) Through the action of heat.

(2) The action of an acid or an alkali, or a solution of a heavy metal (albuminates).

(3) Through the action of ferments, *e.g.*, albumoses and peptones.

3. Conjugate or complex proteids.
   - Nucleo-proteids.
     - Pseudo-nucleo-proteids.
   - Gluco-proteids.
   - Chondro-proteids.
   - Pigment-proteids.
4. Albuminoids, *e.g.*, collagen, chondrin, elastin, keratin, &c.
5. Protamins.

Simple or native proteids are of two types—albumins and globulins. The albumins are soluble in distilled water, and are readily coagulated by heat, more especially in the presence of a little dilute acid; on the other hand, they are not precipitated by saturation of the solution with either sodium chloride or magnesium sulphate, though precipitations occur on complete saturation with ammonium sulphate. The two chief members of this group are egg- and serum-albumin.

Egg-albumin.—A solution can be readily prepared by separating the white of an egg from the yolk, and after dividing the membranes and filtering, shaking it up with twenty times its volume of water. The solution yields a very distinct coagulation with nitric acid, tannic acid, picric acid, the solutions of the salts of the heavy metals, such as the salts of lead, silver and mercury, and with alcohol. It is also coagulated by ether, a reaction which differentiates it from serum-albumin.

It has a lævo-rotatory power of 35·5°, and coagulates at a temperature of from 70 to 73°C.

Serum-albumin has a rotatory power of 56°, and it is not so easily coagulated with alcohol, while the precipitate obtained by the action of strong hydrochloric acid is readily dissolved on adding an excess of the reagent, whereas in the case of the egg-albumin the precipitation becomes more marked. It has been shown that there are apparently several albumins in the blood which coagulate at different temperatures, namely 73°, 77° and 84°C. respectively; after removal of the salts from the plasma, however, they seem to coagulate at a slightly lower temperature.

The **globulins**, unlike the albumins, are insoluble in distilled water, but are freely so in dilute saline solutions, while they are precipitated by saturation of the solution with either sodium chloride or magnesium sulphate. Like the albumins they are precipitated by complete saturation with ammonium sulphate, and by the action of nitric acid, tannic acid, alcohol and the salts of the heavy metals. Globulins are also precipitated by passing a current of CO_2 through the solution. The most important members of the group are—serum-globulin or paraglobulin, fibrin-

ogen, the globulins of muscle, and the crystallin in the lens of the eye. Both the serum-globulin and the fibrinogen are found in blood plasma, and as they are of great importance we shall consider them in some detail. Both the globulins can readily be separated from the albumins by placing the plasma in a dialyser, immersed in distilled water, when, as the salts diffuse out and the percentage becomes reduced, the globulins are precipitated, while the albumins remain in solution.

Schmiedeberg has given the following formula for serum-globulin :—

$$C_{117}H_{182}N_{30}S_{38} + \frac{1}{2}H_2O.$$

The globulins can also be separated by adding crystals of magnesium sulphate, or an equal quantity of a saturated solution of ammonium sulphate (half saturation), though the exact nature of the precipitate thus obtained has been a subject of great dispute. It seems to consist not only of a true globulin, insoluble in distilled water, but also of an albuminous body (glutolin) which remains in solution.

A ready method of obtaining the paraglobulin is by first freely diluting the plasma (1 in 20) and then passing a current of CO_2.

The fibrinogen, though probably of slight value as a food material, is an all-important factor in blood coagulation. It is present in comparatively small amount in the blood and the lymph.

In many respects it differs very considerably from paraglobulin. Thus, if an equal volume of a saturated solution (35·87 per cent.) of common salt be added to a tube of plasma, it will be found that the fibrinogen becomes precipitated, while the paraglobulin remains in solution, or, in other words, a strength of 17·9 saline precipitates fibrinogen while a percentage of at least 20 is required to precipitate the paraglobulin. Again, the coagulation temperatures of the two globulins are very different, the serum-globulin being coagulated at 75°C. and the fibrinogen at the extremely low temperature of 56 to 58°C.

Globulins of muscle.—We have certainly one globulin in muscle plasma, called by Halliburton paramyosinogen and by v. Furth myosin. There is also a second proteid, however—myosinogen or myogen—which, while it possesses many of the properties of a true globulin, differs markedly in not being precipitated by removal of the salts, and is therefore more commonly placed among the albumins. They can also be separated by the fractional temperature method, as the paramyosinogen coagulates at 47°C. and the myosinogen at 56°C.

These proteids can be obtained by extraction with physiological saline (v. Furth's method). Muscle plasma coagulates spontaneously at ordinary temperature apparently without the action of any ferment.

The paramyosinogen becomes directly transformed into an insoluble substance, called by v. Furth myosin-fibrin, while the myosinogen passes first through an intermediate soluble stage (soluble myogen-fibrin) before reaching its insoluble state, in which, in conjunction with the other insoluble element, it forms the clot.

Crystallin.—This proteid can be obtained by grinding up the lens in a mortar with sand and a little saline, when a watery extract is obtained containing traces of albumin, which can be readily separated by passing a current of CO_2 through the solution, when the globulin is at once precipitated.

Globin.—Though globin is often included among the globulin group of proteids, it differs from them in many respects, thus it is insoluble and requires strong acids or alkalies to convert it into an albuminate.

Modified proteids.—**Albuminates.**—They are obtained by the action of acids, alkalies, metallic salts or the halogens. Acid albumin or syntonin may be prepared by adding a little acid to a solution of egg white, though some little time may elapse before the transformation is completely effected. The process may be slightly accelerated by heating. Acid-albumin is not coagulable on heating, but is at once precipitated on neutralisation, when it can be collected by filtration. It can also be precipitated from the solution by the addition of common salt or magnesium sulphate. In somewhat similar fashion solutions of alkali-albumin can be obtained by adding caustic hydrate to a solution of egg-albumin. The formation, however, is more rapid than that of the acid-albumin. It does not coagulate on boiling. If the solution be then cooled and a little acid added a copious precipitation of alkali-albumin at once takes place.

If strong caustic hydrate be added to an undiluted solution of egg-albumin a curious gelatinous mass is obtained called Lieberkühn's jelly. A somewhat similar compound of acid-albumin is obtained after the addition of a strong acid.

Proteoses and peptones.—These are the most important derivatives of gastric and pancreatic proteolytic digestion, as they are most probably (especially the peptones) the types in which the proteid food materials are absorbed into the intestinal wall.

If a few flakes of well washed fibrin be placed in a beaker containing a little pepsin and dilute hydrochloric acid, it will be noticed that the fibrin first swells up, becoming more transparent,

and later becomes slowly dissolved away, and if portions of this digest be removed at intervals and tested, it will be found that the albuminous reaction disappears from the transformation of the acid-albumin into proteoses and ultimately peptone.

The proteoses or albumoses are generally divided into two classes —the primary and the secondary. The primary forms are called protoalbumose and heteroalbumose, while the secondary contains only one type, namely, deuteroalbumose. We have also a fourth form, called dysalbumose, which is probably an insoluble portion of the primary albumoses.

The proteoses can be separated from the peptones in the digest by saturation with ammonium sulphate, when the proteoses are precipitated, while the peptones remain in solution. A readier method is to dissolve some Witte's commercial peptone (a mixture of albumose and peptone) in water, and then fully saturate the solution with ammonium sulphate.

Separation of the primary from the secondary proteoses.—This can be effected by saturation of the albumose solution with sodium chloride, which precipitates the primary forms, while the protoalbumose can further be separated from the heteroalbumoses by the addition of alcohol. When the solution has acquired one-third alcohol the protoalbumoses are precipitated.

Tests for Proteoses and Peptones.—Both give a very characteristic pink reaction with a trace of copper sulphate and excess of caustic potash (biuret reaction). Nitric acid precipitates albumoses, the coagulum disappearing on the application of heat and reappearing on cooling; with peptones the acid gives no precipitation. Again, complete saturation with ammonium sulphate precipitates albumoses but not peptones. Finally, the peptones are much more diffusible than the proteoses.

Coagulated proteids.—These are produced by the action of heat on native albumin or globulin, and also by neutralisation and heat on solutions of the albuminates. They are insoluble in water, saline solutions and weak acids, though they are soluble in strong acids, and are digested by the action of the gastric and the pancreatic juices.

Conjugate or complex proteids.—Nucleo-proteids.—As the term indicates, these are compounds of nuclein with some form of proteid. They vary somewhat in character according to the type of the nucleic acid and the variety of the associated proteid. One of the simplest forms is found in the spermatozoa of certain fish, such as the sturgeon and the herring, where the nuclein is associated with an extremely simple proteid body called a protamin. Nuclein is peculiarly rich in phosphorus, which, as we shall see later, can be separated from the molecule by prolonged analysis.

Thus, if a watery extract be made of a highly cellular organ, such as thymus or testicle, and a little acid added, the nucleo-proteid is immediately precipitated. It is then subjected to the action of pepsin and hydrochloric acid, when a proteid element becomes separated and converted into albumose and peptone, leaving a residue of nuclein which though insoluble in acid can be dissolved up in alkali. The nuclein is then exposed to the action of strong hydrochloric acid, when a second proteid molecule separates off, leaving a residue of nucleic acid, which after prolonged exposure to the action of the acid and heat breaks up into a series of simpler bodies, which vary considerably with the type of nucleo-proteid under examination, but which generally consist of:—

(1) Phosphoric acid.
(2) Bodies belonging to the purin or alloxuric series $C_5H_4N_4$.
(3) Carbohydrate radicles.

The purin bodies are of the utmost interest, as they form a distinct chain of oxides and amines, all of which are of considerable importance. The oxides are three in number:—

(1) Monoxypurin	.........$C_5H_4N_4O$	.........Hypoxanthin.
(2) Dioxypurin	.........$C_5H_4N_4O_2$	.........Xanthin.
(3) Trioxypurin	.........$C_5H_4N_4O_3$	.........Uric Acid.

The amine and oxyamine are—

(4) Aminopurin	.........$C_5H_4N_4NH$	.........Adenin.
(5) Aminooxypurin	.........$C_5H_4N_4ONH$	.........Guanin.

Adenin is especially obtainable from the thymus nucleins and guanin from those of the pancreas.

The origin of uric acid has been for many years one of the most disputed subjects in Physiology and in Medicine; it is the chief derivative of proteid katabolism in birds and in reptiles, and is found in very small amount in the urine of man. At one time it was very commonly held to be a precedent of urea, as the oxidation of uric acid will produce that substance. Again, uric acid can readily be formed by heating urea with glycin, thus—

$$\underset{\text{Urea.}}{3CO(NH_2)_2} + \underset{\text{Glycin.}}{C_2H_5NO_2} = \underset{\text{Uric acid.}}{C_5H_4N_4O_3} + 3NH_2 + 2H_2O.$$

It is probable, however, that in the body the formation of the two substances—uric acid and urea—are independent of one another, the former being derived from the disintegration of the ingested nucleo-proteids, and the latter from that of the ordinary tissue proteid. The experiments of Horbaczewski and Minkowski confirm the chemical evidence we have just mentioned, for they showed that the amount of uric acid excreted by the animal

Fig. 7.—Urea Crystals.

Separated by slow evaporation from aqueous solution.

Fig. 8.—Calcium Oxalate.

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varied directly with the nucleo-proteid intake, and, further, that the administration of purin bodies greatly increased the excretion of the uric acid.

Pseudo-nucleins.—In certain instances disintegration of the nucleo-proteid molecule by digestion and acids does not liberate bodies belonging to the purin series, though in other respects they may resemble the true nucleins. Of these pseudo-nucleins, caseinogen is an excellent example.

Gluco-proteids.—In this group we have the union of a proteid with a carbohydrate radicle, which can be separated on boiling with dilute acids; in many cases, however, it has been shown that the radicle is not a true sugar, but a nitrogen-containing derivative called glucosamine ($C_6H_{11}O_5NH_2$). Of these gluco-proteids, mucin is the most important. It is found more especially in the alimentary canal, the saliva, bile, synovial fluid, and in embryonic or degenerating connective tissues.

The mucins obtained from these different sources differ somewhat from each other in relation to reagents. Generally speaking, however, they are thick or viscid, soluble in dilute alkalies, and precipitated by acetic acid. When boiled for some time with strong acid (sulphuric acid) they yield leucin and tyrosin. From the presence of the latter radicle they respond to Millon's reagent in addition to the usual reaction with the xanthoproteic test.

Other examples of this class of conjugate proteid are to be found in the colloidal material found in degenerating tumours, in the chondro-mucoid substance of cartilage, and in the curious waxy material—lardacein—deposited in the walls of the blood-vessels, &c., in diseases attended with chronic suppuration.

Pigment-proteids.—Of these the chief examples are hæmoglobin and the histohæmatins.

ALBUMINOIDS.

These resemble the ordinary proteids in several ways; thus they are non-crystalline and colloidal, and on decomposition they yield many of the derivatives, such as leucin, which are characteristic of proteid. Some (such as keratin) contain a very large percentage of sulphur in their molecule, and, finally, they give most of the class reactions peculiar to the proteid group. On the other hand, they have certain well-marked points of difference, both chemical and physiological. Thus albuminoid cannot take the place of native proteids as a food material, as it seems to be incapable of replacing the katabolic changes which take place in the protoplasm of the tissue cells, though, as we shall see later, it can

to a very considerable extent diminish the amount of proteid required by the animal. It is therefore often called a "proteid saver." The most important members of this group are collagen, elastin and keratin.

Collagen is the chief constituent of all white fibrous tissue, and is also found in a slightly modified form in bone (ossein) and as the chondrin of cartilage. It is insoluble in cold water, but on boiling it becomes hydrated into a solution of gelatine, which sets as the temperature falls. It does not give (if the gelatine be perfectly pure) any reaction with Millon's reagent, as it does not contain a tyrosin radicle, though it gives a very distinct purple reaction with copper sulphate and caustic hydrate. It is precipitated by mercuric salts, by tannic acid, and by bromine water, but not by nitric acid or lead acetate. It contains only minute quantities of sulphur. Like true proteids it is precipitated on saturation with ammonium sulphate. Under the action of pepsin and hydrochloric acid it is transformed into gelatine peptone.

Elastin.—An albuminoid found in elastic tissue, such as the ligamentum nuchæ. It is extremely insoluble, resisting the action of water and dilute alkalies and acids. It is slowly digested by the action of pepsin and hydrochloric acid, yielding leucin and tyrosin (*cf.* gelatine).

Keratin is found in epidermic tissues, such as nail, hair, skin, feathers, horn, &c. It is extremely insoluble and is not digested by pepsin and hydrochloric acid. It contains a very large percentage of sulphur, and hence if a little keratin be boiled with caustic soda and a drop of the acetate of lead added, it immediately becomes blackened in colour. On disintegration with hot acids it yields both leucin and tyrosin. In the central and peripheral nervous system we find a slightly modified form of this substance, called neurokeratin. It forms apparently a framework in the medullary sheath of the nerve-fibres.

Protamins.—These are of peculiar interest as they are the simplest form of proteid bodies of which we have any knowledge. They are found in the testis of certain fish, such as the sturgeon, herring and mackeral. Sturgeon protamin, or sturin, has a formula of $C_{36}H_{69}N_{19}O_7$, and Kossel has shown that on disintegration it breaks up into the hexones we have already mentioned, namely, histidin, arginin and lysin, and which apparently form very important nuclear groups in the proteid molecule. Indeed, he holds that the more complex types of proteids consist essentially of these cell groups (hexones) to which various contributory nuclei have been added.

II.—CARBOHYDRATES.

As this type of food material forms a very large and important part of the dietary we must consider it in some detail.

All the carbohydrates contain carbon, hydrogen and oxygen, in definite proportion. In the various types the carbon atoms are present in definite numbers, thus we have the trioses (C_3), tetroses (C_4), pentoses (C_5), hexoses (C_6), &c. Of these, only the pentoses and the hexoses are of any physiological importance.

The pentoses are not infrequently excreted in the urine. The most important members of this group are the arabinoses and xyloses. If the pentoses are injected subcutaneously the greater part is at once excreted unchanged in the urine. It has been found in the urine in diabetes and in various other conditions, such as prolonged alcoholism. They possess the general characters of the hexones, reducing metallic oxides, and forming osazones with phenyl hydrazin. They can be recognised by either the phloroglucin or orcein reactions. Unlike glucose they do not ferment with yeast. It has been found also that the pentoses can be derived from the disintegration of some of the nucleins, more especially those of the pancreas.

The hexoses are, however, the most important class of sugars to the physiologist. They have the formula $C_6H_{12}O_6$, and are generally called the monosaccharids. By the union of two molecules of hexose and the removal of a molecule of water we get a second group of carbohydrates, called the disaccharids, thus—

$$\underbrace{C_6H_{12}O_6 + C_6H_{12}O_6}_{\text{Hexose.}} = \underbrace{C_{12}H_{22}O_{11}}_{\text{Disaccharid.}} + H_2O.$$

Similarly, by the union of a number of hexone molecules and the removal of a corresponding number of molecules of water, we get a large moleculed carbohydrate, called a polysaccharid $(C_6H_{10}O_5)_n$.

Conversely, by hydrolysis, the larger polysaccharid and disaccharid molecules can be transformed into the monosaccharids or hexoses.

Classification of carbohydrates—

Monosaccharids $C_6H_{12}O_6$.
 Dextrose—Lævulose—Gelactose.
Disaccharids $C_{12}H_{22}O_{11}$.
 Lactose—Maltose—Sucrose.
Polysaccharids $(C_6H_{10}O_5)_n$.
 Starch—Glycogen—Dextrins or gums—Cellulose.

The monosaccharids.—The glucoses or hexoses are extremely diffusible substances which are readily absorbed through the

intestinal wall into the portal blood-stream, and which ultimately pass to the tissues, there to be completely oxidised into carbon dioxide and water. They possess a very characteristic power of removing oxygen from various substances, such as metallic oxides, indigo, &c., which is due to the presence of an aldehyde group. This reducing power of the glucose (glucose being the aldehyde of the hexatomic alcohol sorbite) gives us a series of simple tests by which we can determine their presence. Thus, if a solution of glucose be boiled with an alkaline solution of a metal such as cupric sulphate, the cupric hydrate (blue) becomes reduced to the cuprous hydrate and oxide (red). The test can be performed in several ways, which are of such importance that we shall consider them in detail.

Trommer's method.—To a few drops of cupric sulphate add a little of the glucose solution and some caustic hydrate. A blue solution is obtained which turns red or orange-yellow on boiling. If desired a few grains of Rochelle salt can be added to the mixture as it assists in dissolving up the cupric hydrate formed on the addition of the alkali, otherwise on heating the colour change may be somewhat cloaked by the formation of the black oxide.

Fehling's method.—The special reagent employed in the test is a mixture of cupric sulphate and a strongly alkaline solution of Rochelle salts (sodic-potassic tartrate). As it tends to decompose on standing, it is better to keep the two solutions in separate bottles and to mix them as required. The condition of the reagent can be readily tested by boiling before introducing the glucose or suspected fluid.

Barfoed's test.—Barfoed's reagent is made by adding a little acetic acid to a solution of neutral cupric acetate. The test is very useful as the reduction is only effected by dextrose.

A similar reduction with other metallic oxides can be employed if desired, thus if glucose be boiled with a mixture of bismuth subnitrate and sodium carbonate, the salt becomes reduced to metallic bismuth, forming a greyish-black deposit. Again, it will remove the oxygen from indigo blue, rendering it colourless; on shaking up with air the colour returns.

All the carbohydrates are dextro-rotatory, with the exception of lævulose. The angle of rotation varies considerably in the different instances, thus the dextro-rotatory power of glucose is 56°, that of maltose 150°, and that of lactose 52·5°.

A very striking characteristic of many of the monosaccharids and the disaccharids is their power of uniting with phenyl hydrazin, forming in the first place a series of bodies called hydrazones, which later unite with a second molecule of the reagent, forming the osazones.

The test can be carried out as follows :—

One part of phenyl hydrazin hydrochloride and two parts of sodium acetate are added to an equal quantity of a solution of glucose. The mixture is then kept at a temperature of 100°C. for some time; when the solution is cooled crystals of osazone settle out. Glucose, lactose and maltose all form these com-

pounds with phenyl hydrazin. The crystals are very easily obtained in the case of glucose, as they begin to settle out in a very short time and while the solution is still hot. The malt and lact osazones, on the other hand, take much longer to form (about an hour) and are only precipitated as the solution cools. The various osazones differ in appearance, solubilities and melting points. The glucosazone appears as fine needle-like crystals, frequently arranged in sheaf-like formation, and have a melting point of 205°C. The maltosazone crystals are somewhat similar, but they are somewhat broader and the melting point is 206°; while the lactosazone forms in rounded clusters of very fine spicules, and melts at 200°C.

Fermentation.—All the hexoses and the disaccharid maltose become split up under the action of yeast into CO_2 and alcohol—

$$\underset{\text{Hexose.}}{C_6H_{12}O_6} = \underset{\text{Alcohol.}}{2C_2H_6O} + 2CO_2.$$

Lactose and sucrose only ferment after inversion has taken place.

Dextrose. — Dextrose or glucose is normally found in small quantities in the blood and lymph and in the various tissues of the body. It may be derived either from ingested carbohydrate, or from the breakdown of proteid. The amount of dextrose in the blood, under normal conditions, is extremely small, never exceeding ·2 per cent. In pathological conditions, and after experimental lesions, it may, however, be present in larger amount. When pure it is a white powder, readily soluble in cold or hot water, with a distinctly sweet taste. It gives all the reactions we have already mentioned, namely, it forms a characteristic osazone with phenyl hydrazin, it reduces metallic oxides, it ferments with yeast, and it is dextro-rotatory. When boiled with a caustic alkali, it acquires a sherry-like colour, with a distinct caramel odour. The change is due to the formation of glucic and melassic acids. The test (Moore's), however, is not a very satisfactory one. It can be distinguished from the other reducing sugar by its power of reducing cupric acetate (Barfoed's test).

Lævulose. — This sugar has practically the same reactions as dextrose, and forms a similar osazone with phenyl hydrazin. It can be obtained by the hydrolysis of cane sugar, as it splits into two molecules, one of dextrose and one of lævulose. It can be easily recognised polarimetrically as it is the only lævo-rotatory sugar.

The **Disaccharids.**—Two members of this group, viz., lactose and maltose, resemble the monosaccharids in several respects, thus they can reduce cupric oxide, and form osazones with phenyl hydrazin. Maltose, however, readily ferments under the action

of yeast, while lactose does not do so. Lactose has a feebly saccharine taste and is of considerable weight.

Sucrose, the third member of this group, differs in many respects from the other two, thus it does not form osazones, reduce metallic oxides, nor ferment under the action of yeast. When boiled with a dilute acid it becomes hydrolysed to form two hexose molecules, viz., dextrose and lævulose, while with strong sulphuric acid it gives a characteristic black char. When injected into the blood-stream it is immediately excreted as a foreign body, but when injested it becomes inverted into dextrose and is absorbed in that form.

Polysaccharids.—These are all typical colloids, with a large molecular constitution; they differ very markedly from the monosaccharids and the disaccharids, both in their reactions and in their physical characters. The chief members of this group of physiological importance are:—(1) starch, (2) glycogen, (3) the dextrins or gums, (4) cellulose.

Starch $(C_6H_{10}O_5)_n$.—This is one of the most important constituents of the food, as it forms the essential basis of such substances as potato, rice, &c. It is found in the green parts of plants in the form of granulose, surrounded by an envelope of cellulose. The structure can readily be seen by grating up a potato in water and collecting the white powder, which, from its insolubility falls to the bottom of the glass. On microscopic examination the characteristic concentric markings can readily be seen. On the addition of a little weak iodine the granules become blue, and the markings more distinct. An imperfect opalescent solution can be obtained by the addition of boiling water; on cooling it may form a paste, or if the solution be more dilute a mucilage.

Tests.—The addition of a trace of iodine gives a very characteristic blue reaction, due to the formation of an iodide of starch. The colour is discharged either by heat or by the addition of an alkali, but returns on cooling or neutralization. On hydrolysis with hydrochloric acid and heat the starch becomes converted into glucose and will then reduce metallic oxides in the usual way. It does not ferment with yeast.

Actions of ferments.—If a little saliva or pancreatic juice be added to some starch mucilage, and the mixture kept at a suitable temperature, the opalescence gradually disappears as a result of the more perfect solution of the polysaccharid; after a few minutes, however, the starch becomes changed into dextrins, and still later into reducing sugar. The intermediate stages can readily be shown by removing a little of the mixture at short intervals with a pipette and testing it with a solution of iodine. At first the reaction is blue from the formation of the blue iodide of starch and then red from the action of the reagent on the erythrodextrin, while after the change is complete and the sugar formed no colour reaction can be obtained. Tannic acid gives a yellowish precipitate which disappears on heating.

Glycogen.—Glycogen, or, as it is sometimes called, animal starch, is found chiefly in the liver in the adult animal, though traces are also found in the muscles, blood, &c. It is in much greater evidence in the developing tissues. It can be readily prepared from oysters. It is imperfectly soluble in water, forming an opalescent solution, and if desired may be obtained as a powder by the addition of alcohol, when it becomes precipitated.

Reactions.—With iodine it gives a port wine colouration from the formation of the iodide of glycogen; as in the case of starch the colour is discharged by the action of heat and alkalies. The colour is almost identical to that obtained with erythrodextrin, but glycogen is precipitated by basic lead acetate, while dextrin is not.

Like all the polysaccharids it neither ferments with yeast nor reduces metallic oxides. Glycogen can be converted into glucose either by boiling with dilute acids or by the action of an amylolytic ferment, such as the amylopsin of the pancreatic juice or the ptyalin of the saliva. Certain ferments also seem to exist within the liver which normally exert a glucolytic action.

Dextrins or gums. — These are much more soluble than the starches, forming with water either a colourless or a pale yellow solution with a distinct gum-like odour. With iodine it gives a reddish-brown colouration closely resembling, as we have already mentioned, the reaction obtained with glycogen. It is not precipitated with either basic lead acetate or tannic acid. There are two dextrins, one which gives the characteristic reaction with iodine, and is therefore called erythrodextrin, and a second which does not give this reaction (achroodextrin). The latter, according to Linter and others, is a later product of the transformation process of starch to sugar.

Cellulose.—Cellulose forms an important factor in the dietary of the herbivora; in man, however, it is of very little importance, from its extreme indigestibility. It is transformed by the action of strong acids into glucose.

III.—FATS OR GLYCERIDES.

Fats are formed by the union of a fatty acid, such as palmitic, stearic, or oleic acid, with glycerine. They are insoluble in water but dissolve in hot alcohol, ether and chloroform. The fatty acids can be obtained by an oxidation of the various monatomic alcohols, which are first transformed to the aldehyde and later to the corresponding acid. Thus from ethyl alcohol C_2H_6O we get the aldehyde C_2H_4O and acetic acid $C_2H_4O_2$.

Of the three acids we have mentioned, palmitic and stearic belong to this fatty series ($C_nH_{2n}O_2$), the palmitic acid being $C_{16}H_{32}O_2$ and stearic acid being $C_{18}H_{36}O_2$. Glycerine is a triatomic alcohol, $C_3H_5(OH)_3$. The hydrogen atoms in the hydroxyls become replaced by the *radicle* ($C_nH_{2n}O_2 - OH$) of the fatty acid, thus in palmitin it has the formula—

$$C_3H_5\begin{cases} O\ C_{16}\ H_{31}\ O \\ O\ C_{16}\ H_{31}\ O \\ O\ C_{16}\ H_{31}\ O \end{cases}$$

Olein is not a member of the ordinary fatty series, the formula is—

$$C_{18}H_{34}O_2(C_n\ H_{2n-2}O_2).$$

In the presence of certain agents such as potassium or sodium hydrate they are split up into glycerine and a fatty acid, the latter uniting with the alkali to form a soap, thus—

$$\underset{\text{(Tristearin)}}{C_3H_5(C_{17}H_{35}COO)_3} + 3KHO = \underset{\text{(Potas. stearate)}}{3(C_{17}H_{35}CO.OK)} + \underset{\text{(Glycerine)}}{C_3H_5(OH)_3}.$$

The three neutral fats, in varying proportions in different animals, form the deposited fats of the body. Thus in a hard fat, such as mutton fat, the proportions of the harder fats tristearin and tripalmitin is considerably greater than in dog or human fat, which contains a higher percentage of olein. Digestion of fat in the intestinal canal is entirely due to the action of the steapsin of the pancreatic juice. The ferment primarily splits up the fat into glycerine and fatty acid, and a small proportion goes on to the formation of soaps. The bulk of the fat is, however, absorbed in the form of the fatty acid and glycerine.

Acids of the glycolic and oxalic series.—These include lactic, sarcolactic, oxalic and succinic acids.

Lactic acid ($C_2H_4(OH)CO.OH$) is prepared from the lactic fermentation of a solution of cane sugar. It is found in the body in the contents of the stomach and intestines, especially after a diet in which the carbohydrates greatly preponderate. Sarcolactic acid is chemically similar to lactic, but physically somewhat different. It is found in muscle, more especially after prolonged contraction.

Oxalic acid $(CO.OH)_2$ is found in combination with calcium, and not infrequently as a urinary deposit. The crystals are extremely characteristic from their small size, octahedral shape and glittering appearance. Less frequently they are of a dumb-bell shape.

Succinic acid $(C_2H_4(CO.OH)_2$ is found in hydrocephalic, hydrocele and hydatid fluids, and also in the spleen, liver, thymus and thyroid glands.

Complex azotised fats and their derivatives.—Lecithin ($C_{44}H_{90}NPO_9$) or

$$C_3H_2=(C_nH_{2n-1}O_2)^2$$
$$O.PO.(OH).O.C_2H_4N(CH_3)_3OH.$$

is found in every part of the body, but more especially in the blood corpuscles, the central and peripheral nervous system, and seminal fluid. On decomposition with acids, alkalies, or digestive juices, it yields a number of bodies, of which the most important are cholin and glycero-phosphoric acid ($C_3H_9PO_6$). Mott and Halliburton have shown that in diseases of the nervous system associated with degenerative changes, such as disseminated sclerosis and general paralysis of the insane, there is an accumulation of cholin in the cerebro-spinal fluid and blood. In the nervous system, the lecithin is combined with a glucoside — cerebrin—forming a complex body called protagon, which can be readily extracted from nervous matter by hot alcohol. Cerebrin, unlike lecithin, contains no phosphorus, and can be obtained by treating the hot alcoholic cerebral extract with boiling baryta water.

Fig. 9.—Crystals of Hæmoglobin.

a, *b*, of man; *c*, of cat; *d*, of guinea-pig; *e*, of hamster; *f*, of squirrel.

THE PIGMENTS OF THE BODY.

1. Hæmoglobin and its derivatives.

(1) Hæmoglobin ("reduced hæmoglobin") occurs in the red corpuscles of venous blood, and in still greater quantity in the blood of asphyxiated animals. It may be prepared from a solution of oxyhæmoglobin by the addition of a reducing agent, such as Stokes'

fluid* or ammonium sulphide, followed by the application of gentle heat. When decomposed by caustic alkali in the absence of oxygen it splits up into the proteid globin and hæmochromogen; if oxygen be present, hæmatin is formed instead. The spectrum of reduced hæmoglobin is shown in Fig. 11. It exhibits one absorption band extending from Fraunhofer's D line, which it touches, nearly to E. (2) **Oxyhæmoglobin** gives the brighter red colour to arterial blood. Venous blood when shaken up with air rapidly takes up oxygen, and the hæmoglobin becomes converted to oxyhæmoglobin. It crystallises in various rhombic forms (Fig. 9) which differ in shape and size in different animals. The accompanying illustration shows a few of these varieties.

They are light yellow in colour, and may be prepared by mixing a drop of blood with a little water on a slide, and allowing evaporation to take place, when the crystals appear at the edge. Oxyhæmoglobin is composed of the elements C H N O S together with Fe. The loosely-combined oxygen is readily removable from it, either by the passage of a current of a neutral gas or the addition of a reducing agent followed by gentle warmth.

Its place may also be taken by other substances, such as carbon-monoxide, and with these it forms more stable compounds. On heating a solution of oxyhæmoglobin with acid or alkali it splits up into the proteid globin (as in the case of reduced hæmoglobin) and acid-hæmatin or alkali-hæmatin respectively. Its spectrum varies with the strength of the solution. Thus a solution ·8 per cent. in strength yields one broad absorption band extending from Fraunhofer's D line to some little distance beyond E (see Fig. 11). With a weaker solution (·3 per cent.) the single band becomes divided into two, and as the solution is progressively diluted these become narrower and ultimately disappear. It will be seen from the figure that the band nearest D is the sharpest and narrowest. (3) **Carbon-monoxide hæmoglobin** is obtained by passing a stream of carbon-monoxide gas through blood or a solution of oxyhæmoglobin; the loosely-combined oxygen giving place to a molecule of CO, which forms a more stable compound with the hæmoglobin. It is this stability which hinders its elimination from the lungs and gives its peculiar danger to poisoning by charcoal fumes. The colour of blood so charged with CO gas is a bright cherry red. The spectrum of CO hæmoglobin is very similar to that of oxyhæmoglobin, as will be seen in Fig. 11, but it differs in the important particular that it is not affected by the addition of a reducing agent, the bands still remaining separate. If a current of nitric oxide gas be passed through a solution of carbon-monoxide hæmoglobin, **nitric-oxide hæmoglobin** is formed by the replacement of the CO by the NO, which forms a still more stable compound with the hæmoglobin. (4) **Carbon-dioxide hæmoglobin.**—When CO_2 is passed through a solution of hæmoglobin, the

Fig. 10.—Crystals of Hæmin.

* Stokes fluid.—Tartaric acid is added to a solution of sulphate of iron (ferrous sulphate), followed by the addition of ammonium hydrate till the solution is alkaline. It must be freshly made.

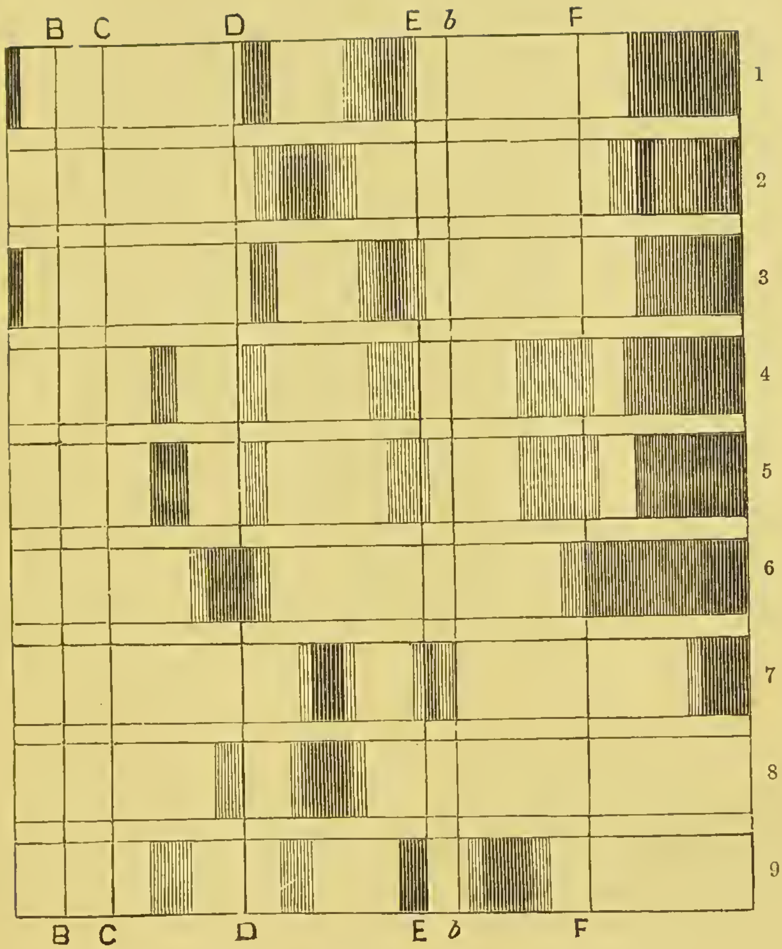

Fig. 11.—SPECTRA OF HÆMOGLOBIN AND DERIVATIVES.

B, Oxygen line; D, Sodium line; C and F, Hydrogen lines; *b*, Magnesium line. 1, Spectrum of oxyhæmoglobin; 2, reduced hæmoglobin; 3, carbonic oxide hæmoglobin; 4, methæmoglobin (in acid solution); 5, acid-hæmatin (in ethereal solution); 6, alkaline hæmatin; 7, hæmochromogen; 8, hæmatoporphyrin (in acid solution); 9, hæmatoporphyrin (in alkaline solution).

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latter appears to split up with the formation of hæmochromogen, which then unites with the carbon-dioxide to form carbon-dioxide hæmoglobin. (5) **Acid and alkali-hæmatins.**—When a solution of oxyhæmoglobin is treated with sulphuric acid or caustic potash and then gently warmed it splits into a proteid and hæmatin, in the former case acid-hæmatin, and in the latter alkali-hæmatin. Hæmatin has the qualitative composition C H N Fe O. Alkali-hæmatin shows one absorption band to the left. *i.e.*, the yellow side of the D line, while acid-hæmatin shows one between C and D, but close to C. Solutions of alkali-hæmatin are dichroic, while those of acid-hæmatin are monochroic. (6) **Reduced alkali-hæmatin** is obtained by adding a reducing agent to a solution of alkali-hæmatin. It is characterised by two absorption bands; one a sharply-defined one between D and E, another less distinct on the blue side of E. (7) **Methæmoglobin** is formed when putrefactive changes take place in blood. It may be prepared artificially by the action of ferrocyanide of potassium or potassium permanganate upon a solution of oxyhæmoglobin, followed by the application of gentle heat and subsequent acidulation. It is probably of the same composition as oxyhæmoglobin, the oxygen being combined in a more stable manner. It shows a characteristic absorption band between C and D. (8) **Hæmochromogen**, as already stated, is formed when reduced hæmoglobin is decomposed by caustic alkali in the absence of oxygen. (9) **Hæmin**, the hydrochloride of hæmatin, is obtained in crystalline form by heating powdered, dried blood with a crystal or two of common salt and a drop of glacial acetic acid under a cover-glass upon a slide. The resulting crystals are small, rhombic in form, and deep brown in colour, contrasting in this respect with those of hæmoglobin. (10) **Hæmatoporphyrin**, composed of C H N O, may be obtained by treating hæmatin with strong sulphuric acid, which dissolves the iron. It is thus an iron-free pigment. (11) **Hæmatoidin** is found in old blood-clots and occurs in hæmaturia; it is probably identical with bilirubin, and occurs in the form of rhombohedral crystals. It is also iron-free.

2. Histohæmatins.

This is the name applied to pigments associated with the tissues. They are examined spectroscopically either by compressing a thin strip of the tissue, *e.g.*, muscle, or by obtaining a solution of the juice of the tissue by treating it with excess of ether. The best known of these histohæmatins is myohæmatin. They seem to have the same respiratory functions as the pigment of the blood in relation to the tissues with which they are associated.

3. Bile Pigments.

(1) **Bilirubin** ($C_{16}H_{18}N_2O_3$), to which the red colour of bile is due, and (2) **biliverdin** ($C_{16}H_{18}N_2O_4$), which is green, are the chief of these. Bilirubin is readily converted to biliverdin by oxidation. It is found forming a great part of gall stones, and in the urine in jaundice. It is insoluble in water, soluble in alkalies, and slightly so in ether and alcohol; but readily soluble in carbon disulphide and chloroform. Biliverdin differs in being very soluble in alcohol, but insoluble in disulphide of carbon or chloroform. Both of them in solution give Gmelin's test, *i.e.*, on the addition of yellow impure nitric acid a play of colours is observable at the junction of the fluids, passing from green through blue, violet, and red to yellow. The blue is due to bilicyanin resulting from the oxidation of biliverdin, the red to bilipurpurin, while the final yellow is due to a still further oxidation product—

choletelin. Hydrobilirubin ($C_{32}H_{40}N_4O_7$), which is probably identical with the urobilin of the urine, can be prepared by dissolving bilirubin in dilute alkali and treating the solution with sodium amalgam. The identity of this substance with urobilin is of great interest as it forms a link in the relationship between the biliary and urinary pigments, and their almost certainly common origin from the colouring matter of the blood.

4. Urinary Pigments.

Urobilin ($C_{32}H_{40}N_4O_7$) may be extracted from urine by shaking it up with chloroform or ether and allowing the solution to evaporate. It is then left as a yellowish-brown powder, which is considered identical with hydrobilirubin. Other urinary pigments are uroerythrin, urohæmatoporphyrin, humus pigments, urinary melanin, indoxyl, and skatoxyl pigments.

5. Melanin.

As found in the skin and in melanotic tumours. Also as the pigment fuscin or retinal melanin. A similar pigment is found in the choroid and iris.

6. Lipochromes, or fatty pigments, include—

(1) Lutein, found in the *corpora lutea* of the ovary, from which it may be extracted by treatment of the tissue with chloroform. It also occurs in egg yolk. (2) Serum-lutein, to which the yellow colour of blood serum is due. (3) Tetronerythrin, which does not, however, occur in man.

7. Rhodopsin.

The visual purple of the retina is found only in the outer segment of the rods. It is characterised by its extreme instability. It is rapidly bleached by white light—even by electric light—and requires to be prepared by the aid of a sodium flame.

CHAPTER II.

THE PHYSIOLOGY OF THE TISSUES.

THE ANIMAL CELL.

A MATURE animal cell consists of two parts—the *nucleus* and the *perinuclear protoplasm.* The latter consists chemically of proteids, carbohydrates, fats, salts and water; and structurally of a network of *spongioplasm*, enclosing in its meshes the fluid *hyaloplasm* or *enchylema.* In such a cell as the amœba, when movement takes place the hyaloplasm at one point first flows out from the meshes of the spongioplasm, which follows it more slowly, thus forming a *pseudopodium.* If the cell be stimulated, the process is withdrawn and the spherical state resumed. This probably corresponds to the contracted state of a muscular fibre, the pseudopodic to the extended state. As in the body generally, so in the cell itself—the ultimate unit—chemical changes take place, both of an anabolic and a katabolic kind. New matter is taken up from the surrounding medium and elaborated to replace the worn-out parts, while effete matter is constantly being thrown out. By the substances taken in it also renews its energy, and gives out energy in other forms; and it possesses the most important of all the functions of animal life, the power of reproduction. The cell may acquire a cell wall, or as it is called a *periplast*, and this may vary from a mere surface condensation of the protoplasm itself to a definite envelope, or even an intercellular hyaline or fibrous matrix.

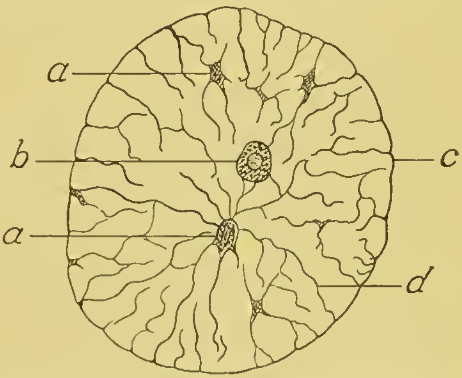


Fig. 12.—The Resting Nucleus.

a, Node of network; *b*, nucleolus; *c*, nuclear membrane; *d*, nuclear network.

The periplast has been variously considered to result from a process analogous to secretion on the part of the cell or to a direct transformation of the protoplasm itself.

The **Nucleus** of the cell is usually round or oval, and consists of a network of *chromoplasm* enclosing a more or less fluid substance, the *nuclear matrix*, the whole enclosed by a distinct wall or *nuclear membrane*. In the nucleus are to be seen one or more *nucleoli*, which have been regarded as merely nodes in the nuclear network, and, on the other hand, as being distinct in function and composition from the rest of the nucleus. Within the nucleoli, *endonucleoli* may sometimes be seen. The chromoplasm consists of a homogeneous ground substance, which does not stain with reagents, and is hence named *achromatin*, in which granules of a readily-stainable substance — *chromatin* — are embedded. The nucleus has probably an important part to play in the nutrition of the cell, and most certainly in its reproduction by division.

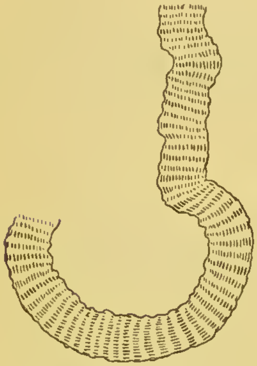


Fig. 13.—Part of a Chromoplasmic Filament.

DIVISION OF CELLS.

Fission, either *direct* or *indirect*, is the method by which cells are usually reproduced in the animal body; and of the two, indirect fission, or, as it is sometimes called, *mitosis* or *karyokinesis*, is much the more common.

Mitotic changes in a dividing cell.—At first the nucleus is in a resting state, the chromoplasm being arranged in the form of a network. This constitutes *the first*, or *network stage*, the condition in which it is found before the process of division becomes initiated. *The second*, or *convolution stage*, is characterised by the nucleus becoming enlarged, and its

Fig. 14.—Diagram of Nucleus, showing the arrangement of the Chief Chromatic Filaments.

a, Primary chromatic filaments; *b*, nucleolus; *c*, node of meshwork.

network, nuclear membrane, and nucleoli assuming the form of a convolutive thread. The thread, narrow at first, and with still narrower filaments branching from it, in a little time broadens from retraction of the filaments, and a more open and less dense appearance results, enabling the individual thread to be more clearly traced. This is followed by *the third*, or *wreath stage*, in which the convoluted thread becomes arranged as a wreath or spirem, and this in its turn gives way to *the fourth*, or *monaster stage*. In this the loops of the wreath break at their periphery, giving rise to a number of V-shaped filaments, separate from each other and arranged radially with their apices towards the centre of the nucleus. At this stage, or a little earlier, the "achromatic spindle" derived from the original "attraction sphere" in the parent cell appears, and the V-shaped loops or "chromosomes" are arranged radially around its broadest or equatorial plane. All cells appear to possess in addition to a nucleus a minute particle or "centrosome" which attracts the protoplasmic fibrils in its vicinity, the whole being termed the "attraction sphere." It is especially prominent in dividing cells, and its division into two accompanies the division of the chromatin, giving rise to the achromatic spindle. At each end of the achromatic spindle is found a "polar particle," from which another cone of achromatic fibrils radiates in an opposite direction. *The fifth*, or *dyaster stage*, is of considerable interest, and is initiated by a longitudinal splitting of the V-shaped loops. This commences at their apices, the split halves immediately becoming turned towards different poles in the spindle, along the threads of which they progress until they reach the pole, where they become arranged in a star-like manner, similar to the unsplit loops in the mother or mono-star. Thus each daughter nucleus possesses

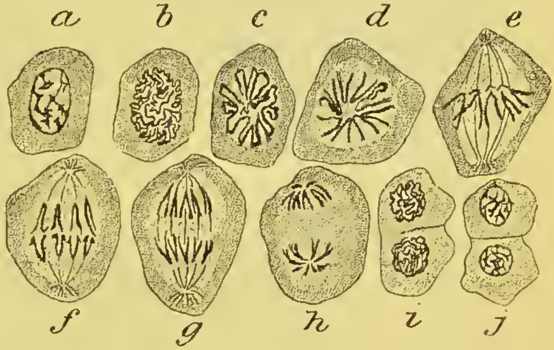


Fig. 15.—Diagrammatic Representation of Stages of Karyokinesis.

a, Cell with resting nucleus; *b*, convolution stage; *c*, wreath stage; *d*, monaster stage; *e*, monaster stage with nuclear spindle with polar zones at its extremities (equatorial plate stage); *f*, splitting of chromosomes; *g*, chromosomes, after splitting, proceeding to poles of spindle (metakinesis); *h*, dyaster stage; *i*, convolution stage (daughter cells); *j*, resting stage (daughter cells).

the same number of chromosomes as the parent; and the number is not accidental, but special to the species. The following stages are merely repetitions of those already described, but in the reverse order. Each daughter star becomes first a wreath, then a convolution, and then the resting stage is attained. The protoplasm of the cell then divides and we have two complete daughter cells produced.

It is to be noted that the nuclear wall disappears at an early stage, to take part in the formation of the convolution or skein, and at the same time the nucleus gives an appearance of "clearing,"

Fig. 16.—Epidermis of Young Salamander.

a, Superficial cells of epidermis containing pigment; *b*, cell more deeply placed, showing resting stage of nucleus; *c*, convolution stage; *d*, wreath stage; *e*, monaster stage; *f*, dyaster stage; *g*, convolution stage in daughter cells; *h*, pigment cells beneath epidermis.

caused by the retraction of the delicate lateral filaments into the main thread of the convolution, thus allowing the clear nuclear matrix to be more in evidence; and that this is accompanied by a clearing of the perinuclear part of the protoplasm itself. The chromatin of the nucleus is said to be identical with *nuclein*, and the achromatin and nuclear spindle are said to be composed of *linin*.

It is to be observed, also, that though the above is a typical instance of indirect division, the chromatin does not invariably form loops, but in some cases rounded particles. The formation of V-shaped loops is very beautifully seen in the growing epidermis of the tail of salamander larvæ.

The **Ovum.**—All the tissues of the body are developed from the *ovum*, which may be taken as an example of a typical cell. The different parts which have received special names are shown in the accompanying figure.

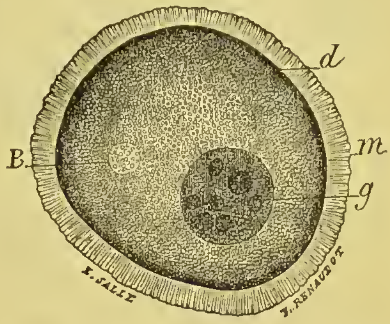


Fig. 17.—OVUM OF MOUSE.

m, Zona pellucida; *g*, germinal vesicle; *d*, cell protoplasm (yolk); *B*, attraction sphere.

The character of the karyokinetic changes preceding its impregnation, both in itself and the spermatogenic cells of the testis, are of great interest, in showing the way in which the number of the chromosomes special to the species is maintained. The process is termed "reducing division," and may be thus described:—The spermatogenic cell of the second layer in the testicular tubule, when about to give rise to spermatoblasts, divides in the usual manner by indirect fission, in which splitting of the V-shaped loops (or chromosomes) occurs to form two daughter cells of the *first generation*, in each of which the chromosomes are of the same number as in the parent cell. While still in the dyaster stage, the chromosomes of the daughter cells themselves undergo splitting, to form a *second generation*, in which the number of the loops is still maintained. The cells of this generation again divide without reaching the resting stage, but this time without splitting of the chromosomes, so that the *third generation* possesses only half the number characteristic of the species. Thus if four be the number, the original spermatogenic cell acquires eight by splitting, and of these four go to one daughter cell and four to the other. Each of these daughter cells doubles its number of chromosomes by splitting in the same way, so that the cells of the immediately succeeding generation (the second) still possess the species number — four. These cells, however, divide without splitting of their loops, so that the cells of the third generation (those whose nuclei form the heads of the spermatozoa) contain only half the normal number. In the case of the ovum, the same process of reducing division is carried on, the original cell acquiring eight chromosomes by splitting, of which four go to the first polar body and four remain in the ovum. The first polar body is extruded and lost, and the nucleus of the ovum divides without further splitting of its chromosomes. Of this division the second polar body (also extruded) accounts for one half, while the other, consisting of two chromosomes, remains as the female pronucleus of

the ovum. Thus in an animal whose species number of chromosomes is four, the spermatozoon contains two, and fuses with the female pronucleus, which possesses a similar number. In this way the original number, four, is restored, and it is maintained in all subsequent cleavage by an accompanying splitting of the chromosomes.

After the union of the male and female pronuclei to form the nucleus of the impregnated ovum, cleavage of both the protoplasm (yelk) and the nucleus takes place repeatedly, giving rise to 2, 4, 8, 16 cells in turn, and the process continues till a mass of *segmentation spheres*, without definite envelope at first, results. The cells by mutual pressure become polyhedral and, by absorption into the ovum of fluid from without, arranged in the form of a membrane, the *blastoderm*, immediately beneath the vitelline membrane. A portion of the blastoderm becomes the *germinal area*, and here by proliferation the layer of cells becomes double, the upper, or outer, layer being termed the *epiblast*, and the lower, or inner, the *hypoblast*. Between the two, in the region of the "primitive streak," a third layer of cells appears—the *mesoblast*. All the tissues of the body are produced from one or more of these three layers, at first formed of similar units which become subsequently differentiated.

The structures of the body include the **simple tissues** (widely distributed, and composed of few individual elements) and the **organs** (elaborate combinations of simple tissues definitely placed in some special region to subserve a particular function). The simple tissues consist either of (1) cells suspended in a fluid, *e.g.*, blood; (2) cells arranged on a free surface, *e.g.*, epithelium; or (3) cells placed interstitially in a matrix, *e.g.*, cartilage. They all consist of cells and intercellular substance. Sometimes the intercellular substance is so small in amount that it merely serves to cement the cells together. Sometimes it forms a matrix widely separating the cells, and it may be supporting fibres. The cells and fibres of any tissue are called the structural elements.

The simple tissues may be considered in the following order:—The blood and lymph; the epithelia; the connective tissues; the muscular and nervous tissues.

THE BLOOD AND LYMPH CORPUSCLES.

The blood consists of a fluid part, the *liquor sanguinis*, in which are suspended the *blood corpuscles*. These are red and white, by far the larger proportion being red. The **red blood corpuscles** in most mammals are non-nucleated, bi-concave discs, in man $\frac{1}{3200}$

of an inch in their broad diameter. They consist of a delicate cell membrane enclosing a network or *stroma*, in the meshes of which, or to some extent in combination with which, *hæmoglobin*, the colouring matter of the blood, is found. The corpuscles are soft and elastic, thus being enabled to accommodate themselves readily to each other and to the exigencies of the passages through which they have to glide when the blood is circulating. Chemical reagents affect the corpuscles in various ways. Under the influence of water or dilute acetic acid they swell up, becoming globular, and the hæmoglobin diffuses out into the surrounding plasma.

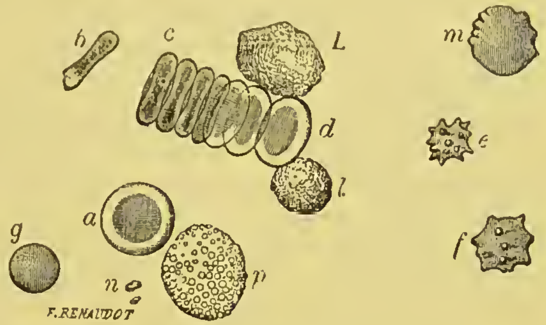


Fig. 18.—Red and White Corpuscles of Human Blood.

a, Red corpuscle, surface view; *d*, the same, three-quarter face; *c*, in profile; *e*, *f*, red corpuscles crenated; *p*, large coarsely-granular white cell; *L*, large finely-granular white cell; *m*, slightly crenated red corpuscles; *g*, spherical red corpuscle; *l*, small white corpuscle; *n*, free granulations.

Salt solution, on the other hand, crenates the cells, fluid passing from them by exosmosis. The corpuscle becomes shrunken and wrinkled and in this condition presents somewhat the appearance of a horse chestnut. There are about 5,000,000 corpuscles in a cubic millimetre of human blood. In amphibians (frog and newt) the cells are much larger than in man and other mammals, and in shape are elliptical, bi-convex, and nucleated. The hæmoglobin is limited to the perinuclear

Fig. 19.—Blood of Frog.

a, Red corpuscle, front view; *b*, *c*, the same seen in profile; *v*, vacuole; *n*, *k*, white blood-corpuscles in spherical condition; *m*, the same showing pseudopodia; *p*, a fusiform cell, probably from the vascular wall.

portion, the nucleus itself being free from it. Under the influence of reagents they act much as those of the mammalia, allowance being made for their physical differences. A solution of tannic acid causes the hæmoglobin to be extruded from the cell in the form of buds or as a granular mass; or it may become collected immediately around the nucleus. With syrup of cane-sugar the corpuscles assume a peculiar leaf-like shape, with a twist upon them. Acetic acid causes them to become decolourised and spherical, the nucleus being very distinctly revealed.

In fishes and birds the corpuscles are much smaller than in amphibians, but like those of the frog and newt are still elliptical, nucleated and bi-convex. Those of the bird are narrower than those of the fish. The members of the camel tribe differ from other animals in their red cells being elliptical and non-nucleated.

The chemical composition of the red corpuscle includes that of (1) the hæmoglobin and (2) the stroma. The empirical formula for *hæmoglobin* appears to be $C_{712}H_{1130}N_{214}O_{245}FeS_2$, so that its molecule is a very large one. Its most important characteristic is its power of uniting with a definite quantity of oxygen to form oxyhæmoglobin in the lungs, and the readiness with which it parts with this oxygen to the tissues. The characters of oxyhæmoglobin and hæmin crystals, the effects of carbon monoxide gas, of acids, alkalies, and reducing agents upon solutions of oxyhæmoglobin, have already been considered.

The amount of hæmoglobin present in the blood is conveniently measured by *Gower's Hæmoglobinometer.* The apparatus consists of two tubes, one of which contains glycerine jelly tinted with carmine to the normal colour of the blood diluted 100 times with water, and the other is graduated in parts of 100. 20 cm. of blood is withdrawn from the finger by a pipette and placed in the graduated tube, which is filled up with distilled water till the tint equals that of the standard mixture. If the diluted blood reaches the mark 100, the percentage of hæmoglobin present is normal, if only 50 it is 50 per cent., if 75 it is 75 per cent., and so for other figures.

The *stroma* may be separated as follows:—If the blood be made "laky" (*i.e.*, darker and more transparent) by dissolving out the hæmoglobin from the corpuscles by dilution with water, and dilute sulphuric acid or acid sodium sulphate be then added to the solution, the swollen up stromata shrivel and may be collected by the centrifuge. They consist chiefly of nucleo-proteid and globulin, with some fats, lecithin and cholesterin.

Tests for Blood.—The presence of blood in minute quantity in medico-legal cases may often be indicated by the micro-spectroscope, the light striking upwards through a deep layer of the solution obtained by soaking the suspected stain, or rather the material it is upon, in water; the depth of the layer having the same effect as concentrating the solution. If the quantity of blood present be greater, ordinary spectroscopic examination may reveal the characteristic bands. Microscopically the presence of red corpuscles is of course distinctive, and chemically the formation of hæmin crystals with glacial acetic acid (page 21) is reliable. On the addition of hydrogen peroxide or ozonic

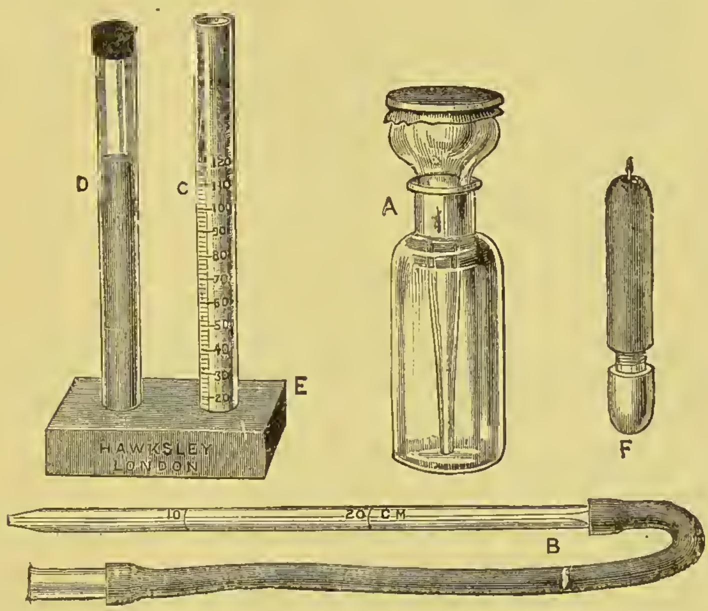


Fig. 20.—HÆMOGLOBINOMETER.

ether to a mixture of the solution of blood and tincture of guaiacum, a blue-green colouration results, and this is a valuable first indication of the presence of blood; but it must not be forgotten that other substances will give the same reaction. No one test should be relied on, but as many as possible employed to confirm the result.

Development of the red corpuscles.—In early embryonic life the red blood corpuscles are nucleated, as they are permanently in birds, fishes and amphibians. They appear to be formed in the following way:—Certain mesoblastic masses of protoplasm, termed *angeioblasts*, branch and form with processes from similar cells

a network representing the future vascular channel. The nuclei proliferate—some remaining in the strands of the network, and others collecting into groups, especially at the nodes.

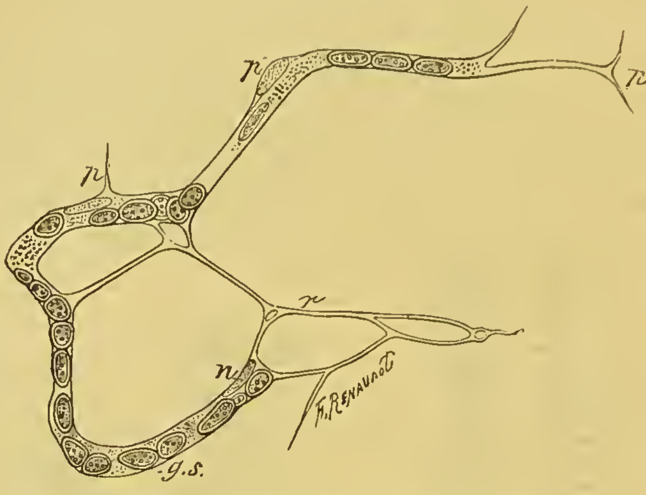


Fig. 21.—Vaso-Formative Network from Great Omentum of Rabbit of Seven Days.

n, Nuclei; *gs*, blood-corpuscles; *p*, protoplasmic prolongations which anastomose with similar ones from neighbouring vaso-formative cells; *r*, network formed from such anastomosis.

The protoplasm immediately around the latter nuclei assumes the characters of the yellow hæmoglobin-bearing stroma of the adult cell, the rest of the protoplasm disappearing by solution. The strands next become hollowed out by a similar process of solution, and an anastomosing network of vascular channels is left, the walls of which are formed of the undifferentiated protoplasm surrounding such of the nuclei as did not take part in the formation of the coloured corpuscles. In later stages of embryonic mammalian life these nucleated cells disappear, and are replaced by non-nucleated ones, which seem to be formed in much the same way, except that the nuclei of the original protoplasmic masses do not appear to take part in the formation of the corpuscles, but only in that of the capillary wall; the corpuscles being formed by the transformation of small portions of the protoplasm to coloured spheres, and the solution of the undifferentiated protoplasm between them.

After birth the formation of red blood corpuscles appears to take place principally in the red marrow of bones, which contains a number of *erythroblasts*, found both in the vascular channels and

among the marrow cells outside them. They are smaller than the marrow cells proper, resemble the nucleated coloured cell of the embryo, and possess to some extent the faculty of amœboid movement. We do not know the process of their transformation to non-nucleated discs before they enter the general circulation, nor from what cells they are immediately derived. They may result from the marrow cells by the acquisition of hæmoglobin, or from division of pre-existing similar cells derived from the nucleated corpuscles of the embryo.

Blood-plates.—These are small, discoid or oval, clear, homogeneous, colourless corpuscles, about a quarter the diameter of the coloured cells, and are sometimes called *hæmatoblasts.* Their significance is not evident. They have been regarded as developing red corpuscles by some, but the evidence is not conclusive.

When mammalian blood is shed, the corpuscles tend to run into *rouleau.* The cause of this is not quite clear. If cork discs are completely submerged in water they do not cohere, but if weighted with tacks and allowed to rise to the surface, so that they are only partially submerged, they are brought together by capillarity. Again, if dipped in petroleum and then placed in water, rouleau are formed. In the case of blood which has been

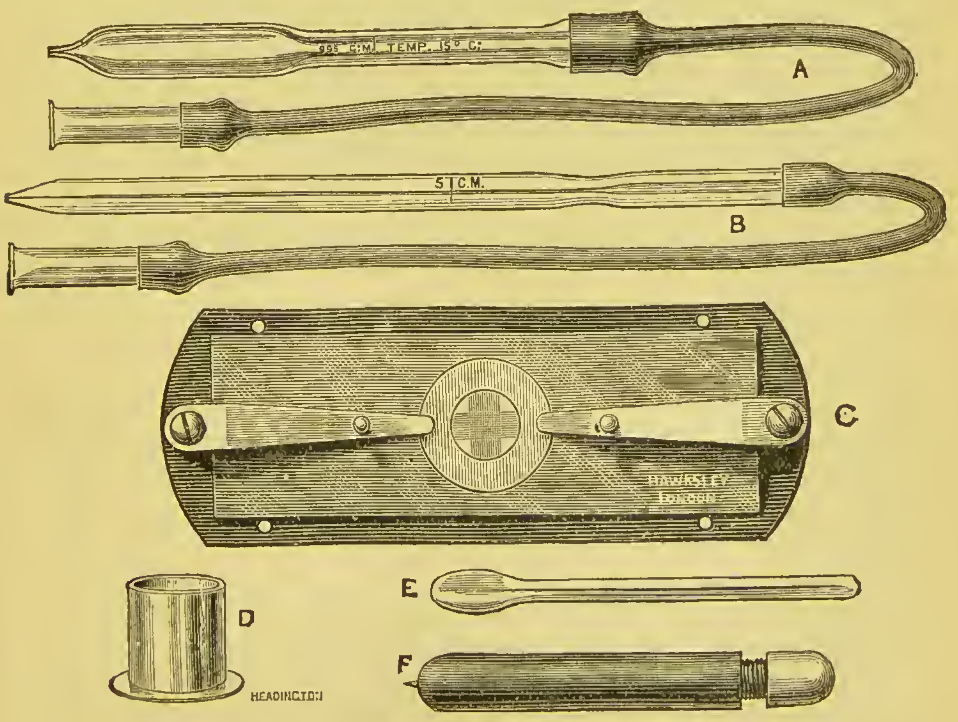


Fig. 22.—Hæmocytometer.

shed the formation of rouleau is probably due to some repulsion between the surface of the corpuscles and the fluid in which they float, with a corresponding attraction of the corpuscles for each other.

The *number of corpuscles* in the blood is readily estimated by the hæmocytometer of Gowers. A known small quantity of blood (5 cm.) is diluted 1000 times with some indifferent fluid (sp.g. 1025) and placed in a cell sunk in a glass slide. The bottom of the cell is ruled in one-tenth millimetre squares, and the cell itself is one-fifth of a millimetre deep. In working with Gowers' hæmocytometer the number of corpuscles in ten squares is counted under the microscope, and the result multiplied by 10,000 gives the number in a cubic millimetre.

The **white blood-corpuscles** are much fewer in number than the red: a cubic millimetre of human blood contains 10,000, as contrasted with 5,000,000 of red. They are fewer than the blood-platelets, which may number 250,000. They are for the most part larger than the red, being often $\frac{1}{2500}$ inch in diameter. They are colourless nucleated masses of protoplasm, possessing the power of amœboid movement. This consists in the power they have to push forward or retract the pseudopodia of their substance. In some cases the body of the cell gradually flows after the pseudopodium, thus enabling it to migrate from place to place. They can also "flow round" any particle in their way, which, if it be suitable for food, is thus ingested and assimilated, and if not it is again cast out. The changes in form of a white cell in a state of amœboid activity may be well studied under the microscope in the blood of the frog; if mammalian blood be used the temperature of the body must be maintained by employing the warm stage. Cold retards and heat quickens the movement up to the point when heat rigor supervenes.

There are several varieties of white blood-corpuscles. The most numerous have a tripartite nucleus, the three parts being united by a narrower band; in others a single nucleus is present, sometimes consisting of a coiled thread. Most of these cells are finely granular, and are termed *the large finely-granular corpuscles.* Others, fewer in number, exhibit in their protoplasm a number of comparatively large clear granules, and are termed *the large coarsely-granular corpuscles.* A third variety is smaller than either of these, and is finely granular, with a single nucleus, large in proportion to the cell, *the small finely-granular corpuscle* or leucocyte. These cells have been classified by Ehrlich, according to their reactions to acid, basic, and neutral stains. In some the granules are stained deeply by stains with acid reaction, such as

eosin, and these he terms "eosinophile"; in some they stain deeply with basic stains, such as acetate of rosanilin, and these are "basophile"; in others with neutral stains, as picrate of rosanilin, "neutrophile."

The amœboid faculty of the white cells is probably of the nature of contractility, "a property belonging to some forms of protoplasm by which its micellæ forcibly assume different relative positions, and so give rise to definite or indefinite changes in the mass" (Rutherford). But whereas in muscle cells contractility is evidenced by shortening, and probably also by lengthening when contraction is over, in the long axis of the cell, in the amœba the various changes in shape are more indefinite, and take the form of protrusion and retraction of pseudopodia. When a muscle cell is stimulated it shortens; when the white corpuscle is similarly treated it resumes its spherical condition. This may be watched under the microscope, as the result of either tapping the cover-glass (mechanical stimulation) or the passage of an electric current. In the blood-stream they are normally spherical, and this condition is probably maintained by the mechanical stimulation of contact with other corpuscles, and with the vessel wall. But when the circulation is slowed to any great extent, as in the stasis stage of inflammation, the amœboid condition is readily resumed. It is by this means that *diapedesis* through the vessel wall into the surrounding tissue is accomplished. As the current slows in the vessel in the injured area, the white cells roll more and more slowly along the inner side of the vessel walls. A cell will then throw a pseudopodium between the epithelial plates, and gradually flow after it till its whole body has passed through. It has then become one of the "wandering cells" of the tissue in which the vessel lies. This process of diapedesis takes place under normal conditions, but to a very much smaller extent. The white corpuscles seem to consist chiefly of a globulin, albumin and nucleo-proteid, salts and water; the salts, like those of the red corpuscles, being chiefly those of potassium and phosphoric acid (*cf.* plasma).

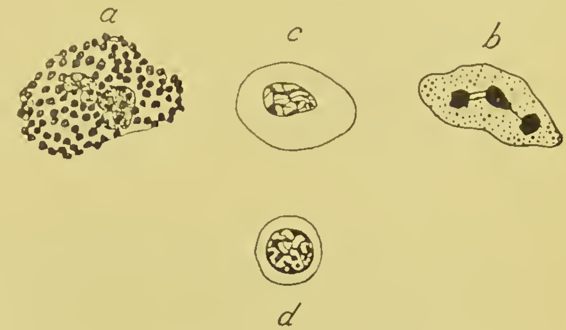


Fig. 23.—Various Forms of Leucocytes.

a, Eosinophile corpuscle; *b*, ordinary polynuclear leucocyte (neutrophile); *c*, hyaline corpuscle; *d*, lymphocyte.

They contain also carbohydrate, fats, and lecithin. They are all probably derived from the lymph-cells in the lymphatic glands and other situations in which collections of lymphoid tissue are found. The tripartite nuclei would seem to show that division of the cells takes place after admission to the blood-stream from the thoracic duct.

The **functions of the white cells.**—They are said to contain the fibrin ferment on which the clotting of blood depends, the ferment being liberated when blood is shed and the white cells begin to break down. Another very important office is that of acting as the scavengers of the body. In this capacity they have been termed *phagocytes* or "eating cells." When any part of the organism is injured, leucocytes immediately repair in vast numbers to the spot to remove the dead tissue by ingestion and assimilation. But foreign substances in the way of bacteria may be there, or in the blood, and often in such a case, if the microbe be virulent and the leucocyte is in an atonic condition and has not become "case hardened" by previous habit, it is apt to die and form a pus-corpuscle in its effort to digest the microbe or its ptomaines.

THE EPITHELIA.

The epithelia, as already stated, consist of cells arranged on free surfaces. The cells are nucleated protoplasts, possessing a cell wall or periplast, and are united to each other by intercellular substance, or *cement*, as it is called, which reduces nitrate of silver. They vary in shape according to the position in which they are found, and occur both in single and stratified layers. They are developed from all the layers of the blastoderm. The epithelium of the skin, nose, mouth, pharynx, eyelids, conjunctiva, and cerebro-spinal cavities is derived from the epiblast; that of the blood and lymphatic vessels, the serous and synovial sacs, the kidney, suprarenal glands, ureter, testis, ovary, uterus and Fallopian tubes from the mesoblast; that of the alimentary canal, lungs, liver, pancreas and bladder from the hypoblast.

VARIETIES OF EPITHELIUM.

1. **Squamous epithelium.**—This is found both in single and stratified layers. (1) *Simple squamous epithelium* lines the great serous sacs, such as the pericardium, pleura and peritoneum, and also the heart, blood-vessels and lymphatics. In these situations

it affords a smooth surface to the structures it covers. It is also found lining the alveoli of the lung, where it aids, or permits of, a gaseous interchange between the air and the blood. It also covers the posterior surface of the cornea and the anterior surface of the iris. The cells are in a single layer, flattened and nucleated, and fitted accurately together by their edges. They differ in contour in different places. Those lining the arteries are elongated, almost fusiform, and slightly sinuous in outline; those lining the veins are broader; in a lymphatic vessel they are the same, but

Fig. 24.—Epithelium of Mesentery of Frog.

c, Outlines of epithelial cells; *m*, large granular cell; *s*, two granular cells with a stoma between them; *p*, two similar smaller cells; *n*, nucleus.

markedly sinuous. Those lining the great serous sacs are polygonal in outline, as are also those in the alveoli of the lung. Wherever simple squamous epithelium is found, the outlines of the cells demarcating them from each other can be very clearly brought out with nitrate of silver. The term "endothelium" has been applied to the forms of simple squamous epithelium lining closed cavities, such as blood-vessels and serous sacs. (2) *Stratified squamous epithelium* is found in the epidermis of the skin, the mouth and nostrils, the lower part of the pharynx, the œsophagus, the vagina and part of cervix uteri, the conjunctiva and the anterior surface of the cornea. It is chiefly protective in

function, but in the case of the cornea and conjunctiva it affords also a smooth surface for the diminution of friction. As its name

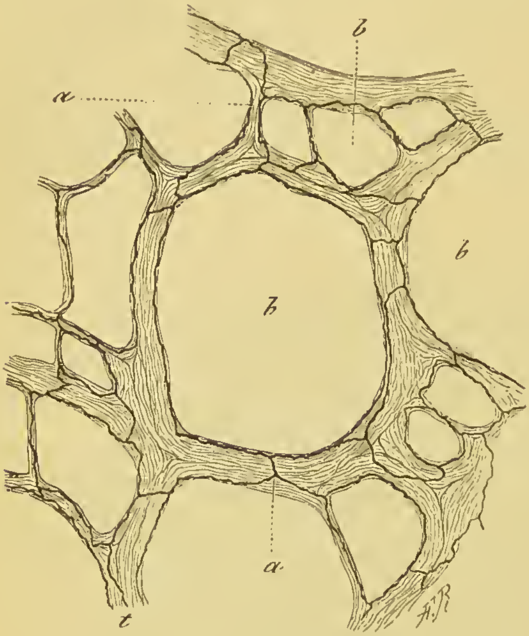


Fig. 25.—Great Omentum of Dog.

a, Junctions of cells revealed by the reagent; *b*, meshes of the network; *t*, fibrous tissue basis of network.

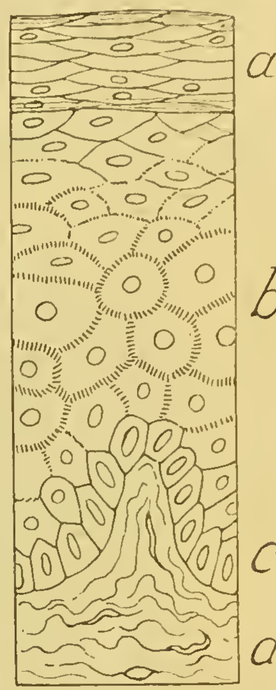


Fig. 26.—Vertical Section of Hard Palate of Cat.

a, Stratum corneum; *b*, soft or Malpighian layer; *c*, germinal layer of cells; *d*, connective tissue.

implies, the cells are in more than one layer; and the shape of the cells in one layer is different from that of those in another. Thus those at the surface are usually flat; those lying deepest, columnar; and those intermediate, polygonal in shape. The epithelium of the hard palate may be studied as an example.

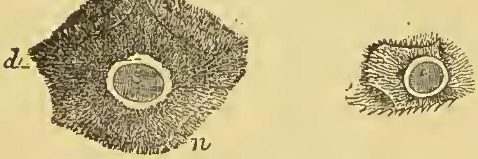


Fig. 27.—Isolated Prickle Cells from the Stratum Malpighii (×880).

d, Nucleus; *n*, prickles.

Here are two subdivisions — the stratum corneum and the stratum Malpighii. The stratum corneum is composed of many superimposed layers of flattened cells, these overlapping each other, and not being accurately fitted together by their edges, as in the simple form. The nuclei have in many disappeared, and the

whole protoplasm has become converted to a horny or corneous substance termed keratin. The stratum Malpighii is composed of softer and younger cells, small and columnar in shape, in the deepest layer of all; and this is called the germinal layer, as it is by division of these cells that those worn off by attrition at the surface of the stratum corneum are replaced. The cells above forming the greater part of the stratum are larger and polygonal in outline. The cells are nucleated, and the polygonal ones especially show the peculiarity of not fitting closely to each other, but of being joined together by "intercellular ridges." An isolated cell with its broken ridges looks as if it were beset with spines, and hence has been termed a "prickle cell." These cells are also characteristic of the Malpighian layer of the epidermis of the skin. The spaces between the ridges form a series of inter-communicating canaliculi, by which the lymph percolates the tissue and secures its nourishment.

2. **Columnar epithelium.**—Columnar epithelium is found lining the alimentary canal from the cardiac end of the stomach onwards, the ducts of the glands opening into it, and in some other situations. It is mostly of hypoblastic origin. In the alimentary canal it is mainly absorptive in function, though some of the cells, however, secrete mucin. As seen in the intestine, the cells occur as a single layer covering the villi. They are columnar in form, arranged palisade-wise, vertical to the basement membrane on which they rest. The outer extremity is broader than the inner, and presents a "striated hem" when seen in vertical section. They are nucleated and possess a cell membrane. Goblet cells are to be seen here and there among the columnar ones, of which they are merely a modification; the whole of the protoplasm, with the exception of a little around the nucleus at the base of the cell, having been converted to mucin, which in being discharged has broken away the cap of the cell, *i.e.*, the striated border. If the columnar cells be isolated from each other they are seen to present lateral wing-like expansions from mutual compression, and the basal end is often very irregular.

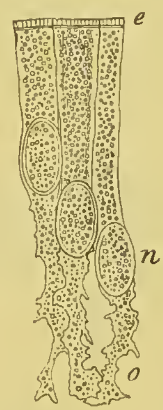


Fig. 28.—Epithelial Cells from Intestine of Frog (× 560).

e, Striated hem; *n*, nucleus; *o*, irregular basal end of cell.

The columnar cells of the stomach are all mucin-forming cells, but are not globular in shape. In these the nucleus, with a little protoplasm, is situated at the base of the cell next to the basement membrane.

The cells lining the ducts of glands are often cubical rather than columnar, and frequently broader at their attached than at their free ends, from the exigence of their position. Those lining the ducts of the salivary glands are vertically striated in their outer part.

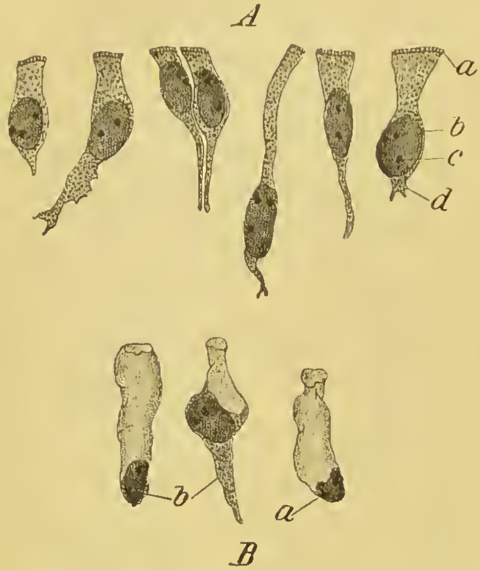


Fig. 29.—*A*. Columnar Epithelial Cells, Dissociated, from Intestine of Newt (× 300).

a, Striated border; *b*, nucleus; *c*, nucleolus; *d*, basal processes.

B. Goblet Cells from same Preparation. *a*, Nucleus; *b*, remains of protoplasm of cell.

3. **Transitional epithelium** is found lining the pelvis of the kidney, the ureter, the bladder, and part of the urethra. Its name is not a good one; it is really a variety of stratified squamous epithelium. The cells are three or four deep—the superficial layer formed of large somewhat flattened and expanded

Fig. 30.—Isolated Epithelial Cells from Bladder of Guinea-Pig (×330).

a. Superficial cell seen from below; *b*, a similar cell seen in profile; *c*, small cells from the deeper layers.

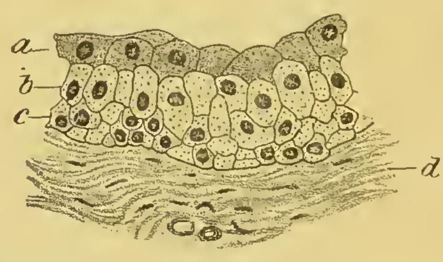


Fig. 31.—Vertical Section of Transitional Epithelium of Bladder of Cat.

a, Superficial layer of cells; *b*, middle layer of cells; *c*, deep layer of cells; *d*, fibrous tissue.

nucleated cells; below this is a layer of polyhedral cells, and last of all the germinal layer, of which the cells are rather pear-shaped and small.

4. **Ciliated epithelium** is found in the respiratory tract, the lachrymal sac and duct, the middle ear, the Eustachian tube, the

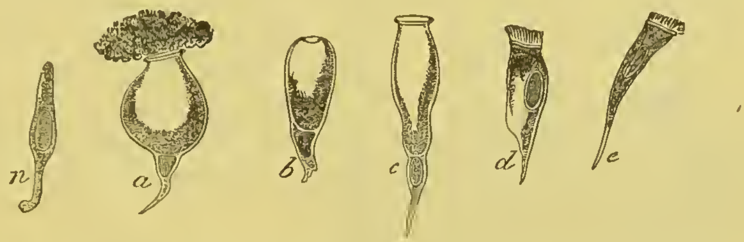


Fig. 32.—ISOLATED CELLS FROM ŒSOPHAGUS OF FROG (×320).

a, *b* and *c*, Mucin-forming cells; *d* and *e*, ciliated cells; *n*, young ciliated cell in which the cilia have not yet developed.

epididymis, the vasa efferentia, the Fallopian tubes and uterus, the cavities and canals of the cerebro-spinal axis (except the 5th ventricle). It is either stratified or simple. In the respiratory system it is stratified, cells of a germinal and intermediate character being found beneath the ciliated cells. Their function is, by means of their cilia, to move fluid over the surface they cover in a definite direction.

A ciliated cell is columnar in form, with a narrow tapering basal extremity (when stratified) and a broad free end. This possesses a highly refractile border, bearing a number of cilia. The cells are nucleated, the oval nucleus being placed in the broader part of the cell. The cilia are flattened pointed filaments $\frac{1}{3000}$ of an inch long, and there are about fifteen to each cell. But they vary in size and number in different situations. They have been especially studied in the mussel, and here each cilium is stated to be attached by a narrow neck or "intermediate segment" to a "basal knob." The knobs in lateral apposition produce the effect of a bright refractile border to the free end of the cell. From each knob a slender varicose thread passes down through the protoplasm of the cell, and,

Fig. 33.—ISOLATED CILIATED CELLS FROM RESPIRATORY PART OF HUMAN NOSTRIL (×750).

avoiding the nucleus, unites with other filaments similarly derived to form a leash at the base.

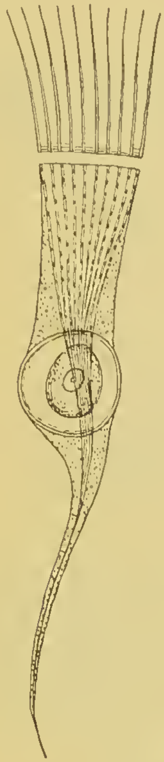


Fig. 34.—Ciliated Cell from the Intestine of a Mollusc.

Ciliary movement is rhythmical, and passes from point to point of the surface, reminding the observer of the bending of a field of corn before the wind. The cilia appear to be contractile on the side to which they bend, the erect position being recovered by the elasticity of the other side. The ciliated cell is automatic, the cilia continuing to bend even when the part containing the nucleus has been torn away, and is thus independent of any local or central nervous influence. Chloroform, ether, carbonic acid gas, and cold suspend or inhibit the action; gentle heat accelerates it. Certain conditions of temperature, oxygen and moisture, are required for its maintenance.

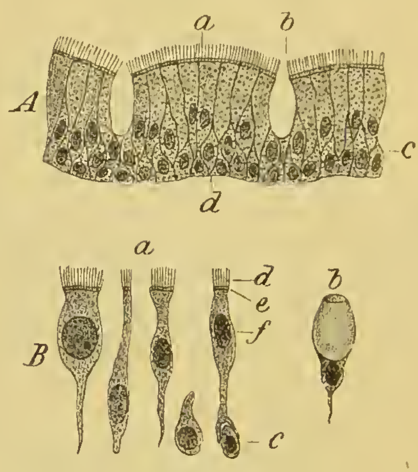


Fig. 35.—*A*. Epithelium of Trachea of Cat (×200).

a, Ciliated cells; *b*, goblet or mucin cells; *c*, germinal cells; *d*, basement membrane.

B. Ciliated Epithelial Cells, Dissociated, from Pharynx of Frog (×300).

a, Ciliated cells; *b*, goblet cell; *c*, cells, germinal, from deeper layer; *d*, cilia; *e*, refractile border; *f*, nucleus.

When the epithelium is stratified, intermediate and germinal cells are present. The intermediate are fusiform in shape, with the nucleus in the broad or central part. As the upper extremity reaches the surface, it acquires cilia, and broadening, takes the place of an older cell which has been cast off. The germinal cells are small and pear-shaped, and lie upon the basement membrane.

5. **Glandular epithelium** forms the tubules of secreting glands, such as the salivary, the liver, and the pancreas. The glands are developed as an invagination of a layer of epithelium, either epiblastic or hypoblastic in origin. It may remain single, or it may become divided and much more complex, but it is always essentially an involution of epithelium communicating directly with the surface, or indirectly through a duct. The cells rest upon a basement membrane continuous with that of the surface from which they were originally derived. The cells vary in shape in different glands. They are nucleated, and usually cubical, polygonal, or somewhat irregular. Their appearance, too, varies with their state of functional activity, being different previous to secretion, when they are loaded, from what it is afterwards, when they are exhausted (see Digestion).

Fig. 36.—Section of Submaxillary Gland of Dog, Exhausted after Four Hours Stimulation of Chorda Tympani Nerve.

g, Gland cells from which the mucus has been discharged, and whose nuclei have increased in size in consequence; *c*, crescent of Gianuzzi.

6. **Sensory epithelium.**—Under this heading may be classed the cells of epiblastic origin which have become specially modified to form nerve terminations, such as the hair-cells of the organ of Corti in the ear, the central cells of the taste buds of the tongue, and the rod cells of the olfactory membrane. These cells of special sense are often rod-like or columnar in shape, and, as in the case of the cells of the auditory apparatus, may possess hair-like processes at their free extremities. By their central or proximal end they are connected with nerve fibrils, by which they are brought into communication with the central nervous system. They are the peripheral plates, in fact, which receive impressions to be carried by the nerve fibres to the sensorium.

The **basement membrane** varies a good deal in structure. Sometimes it is homogeneous and thick, as where it supports the epithelium in the

human trachea and larger bronchi. Sometimes it is much thinner, being merely composed of flattened connective tissue corpuscles cemented together completely or merely by their processes. Sometimes the connective tissue fibres themselves are flattened and expanded to take part in forming the membrane. The tissue outside the basement membrane supports a network of blood-capillaries, and is bathed with lymph. Nerve fibres traverse the tissue and break up into fibrils, previous to piercing the basement membrane, to pass between the epithelial cells or to become directly connected with them.

THE CONNECTIVE TISSUES.

1. **Mucous tissue** represents an early stage in the development of ordinary connective tissue. It consists of a number of delicate-branching nucleated cells, placed in a matrix of mucin. The cells anastomose with each other by their delicate branches, and in some cases fibrils may be seen making their appearance in the mucinous matrix between them. This tissue is found forming the jelly of

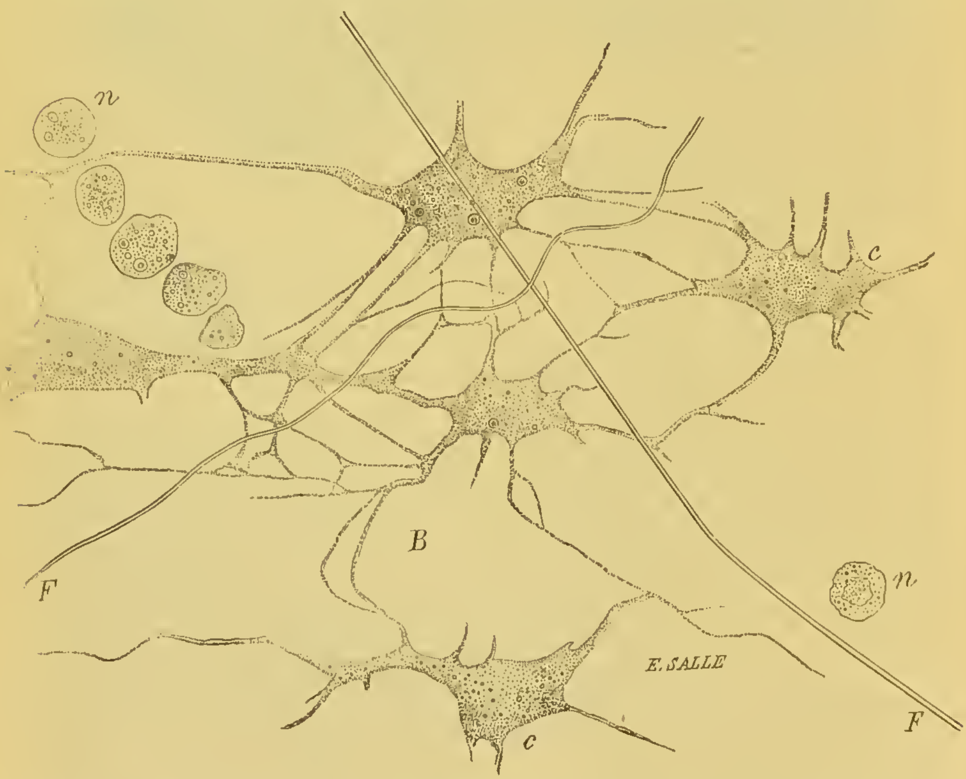


Fig. 37.—Mucous Tissue of Umbilical Cord of Embryo Sheep (×500).

c, Branching cells; *F*, connective tissue fibres; *n*, embryonic or lymph cells; *B*, ground substance.

the umbilical cord in the fœtus, and in the adult the vitreous humor of the eye.

2. **Ordinary connective tissue** occurs in a loosely-arranged form as areolar tissue, and in a more compact one, of which tendons and the ligamenta subflava may be taken as types. (*a*) *Areolar*

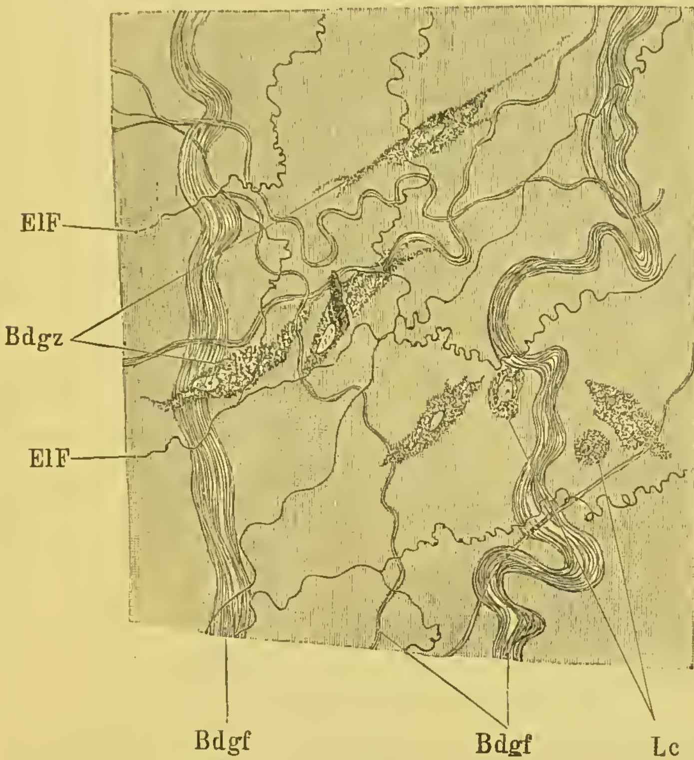


Fig. 38.—Areolar Tissue from Intermuscular Tissue of a Calf (×200).

Bdgf., Connective tissue fibres, *i.e.*, bundles of fibres; Bdgz., connective tissue cells; ElF., elastic fibres; Lc., leucocytes.

tissue is found beneath the skin and many mucous membranes. Its loose elastic structure permits of the free movement of these structures upon the parts they cover.

If the skin of a rabbit's leg be reflected and a little of the filmy tissue lying on the muscles be lifted up with the forceps, it will be seen sometimes as a thin, almost transparent sheet, sometimes as a network of finely-spun glass, the spaces in the network being the areolæ, from which the tissue derives its name. These spaces must not be confounded with the cell spaces

only visible under the microscope in the strands of the tissue itself. The areolæ are normally percolated with lymph.

The structural elements consist of cells and fibres embedded in a mucinous matrix. The cells are of several varieties, of which the most important are—(1) The *fixed connective tissue cells.* They lie in the lacunæ or cell spaces in the mucinous matrix, and are

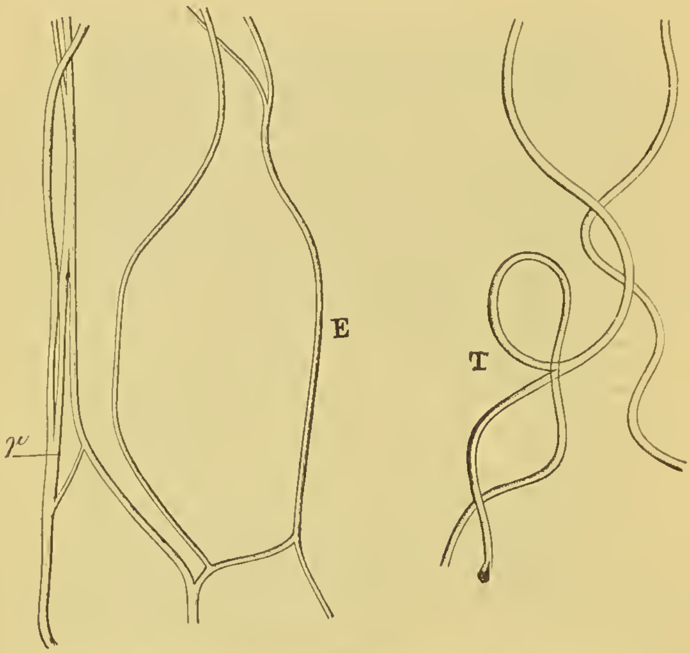


Fig. 39.—Elastic Fibres from Subcutaneous Tissue of Dog (×800).

E, Fibres branching, as at *r*, to form a network; T, isolated fibres pursuing a tortuous course.

nucleated protoplasts, which vary very much in shape. They are often irregular, the branches anastomosing with those of neighbouring cells. If they lie between bundles of white fibres they often give off lamellæ from their sides to pass between the bundles. They may be fusiform and applied to one side of a bundle, or they may be more flattened and bent partially round it; (2) *the coarsely-granular cells*, which are also fixed, surround the vessels where fat is to be developed, as in the neighbourhood of the kidney. They are oval and nucleated, and their protoplasm contains eosinophile and basophile granules; (3) *the plasma cells* resemble the ordinary fixed corpuscles, but have many vacuoli in their cell substance; (4) *the wandering cells*, unlike the preceding,

are not fixed in position in cell spaces. They resemble the small white blood-corpuscles, and traverse the lymph channels.

The fibres are of two kinds—(1) the white; (2) the yellow, or elastic. The *white fibres* are about the breadth of a coloured blood-corpuscle, and are made up of a number of delicate fibrils, about $\frac{1}{5000}$ to $\frac{1}{2000}$ of an inch in diameter, united together by cement substance—the mucinous matrix in which they lie. They are colourless, longitudinally striated, and pursue a tortuous wavy course. A single bundle may divide and its branch coalesce with another, but the individual fibrils do not branch. Under acetic acid the fibres swell up, becoming more transparent and indistinct, and frequently show constricting rings upon them, which have been attributed to the presence of elastic bands, and also to the processes of clasping cells. The *elastic fibres* are much narrower than the white, and bright and refractile. They branch and form an open network, intermingling with the white fibres but separate from them. They pursue a very sinuous course, which is, however, often masked by the stretching of the tissue in preparation, whereby the fibres are made tense and straight. On the addition of acetic acid they stand out clearly from the white fibres, which are rendered more transparent.

The branching cell spaces are clearly revealed by silver nitrate, which is reduced by the mucin matrix, which is rendered dark brown in colour.

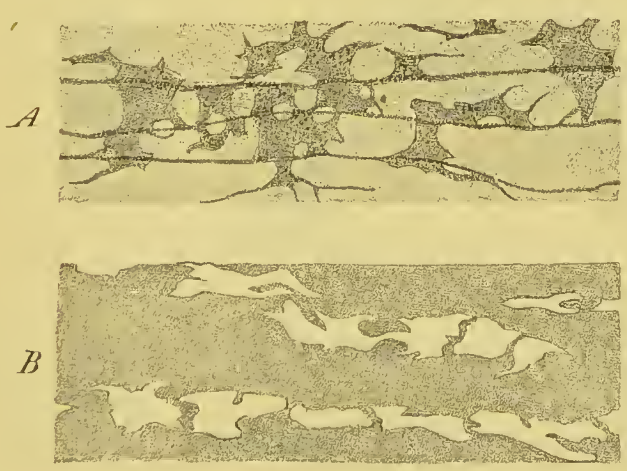


Fig. 40.—Tendon of Rat's Tail.
A, Stained with gold chloride; *B*, stained with silver nitrate.

Ordinary connective tissue is the most widely distributed of any kind of connective tissue, and is found in all parts of the

body. In its loosest form, as areolar tissue, it is found, as already stated, beneath the skin and mucous membranes. In a somewhat denser form it envelops the organs of the body, sending supporting septa into their substance, forms the sheaths of muscles, tendons and nerves, the perichondrium of cartilage, the periosteum of bone, &c. In its most compact form, as where it constitutes tendons and the ligaments, the fibres run parallel with each other in stout bundles. (*b*) *Tendon* is composed principally of bundles of white fibres, with a small admixture of yellow. Between the bundles are placed rows of tendon cells—the fixed cells of the tissue. As in areolar tissue, the fibrils and fibres are united together with cement substance. The cells are nucleated and quadrangular, and give off lateral plates. In

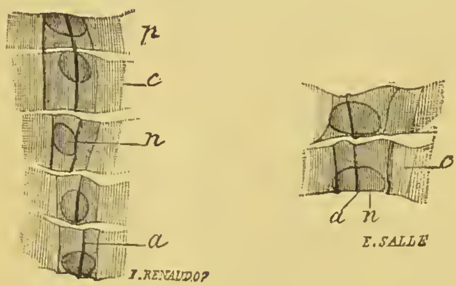


Fig. 41.—Tendon Cells of Tail of Mouse (×325).

c, Cells; *p*, lateral expansions; *n*, nuclei; *a*, Boll's line.

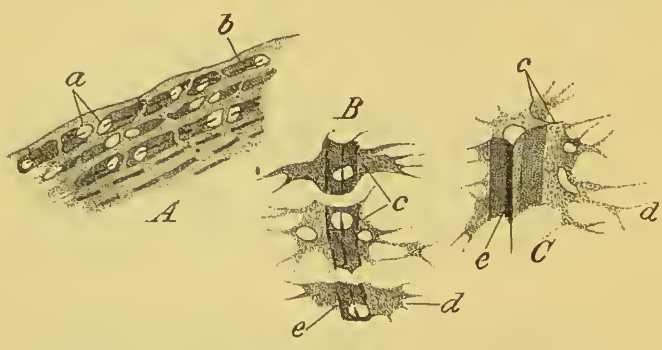


Fig. 42.

A. Tendon Cells of Rat's Tail, as seen in Situ (×150).

a, Nuclei, unstained; *b*, Boll's line.

B. Tendon Cells of Rat's Tail, more highly magnified.

c, Flanges; *d*, processes; *e*, Boll's line.

C. Tendon Cell from Rat's Tail, still more highly magnified (Semi-Diagrammatic).

c, Flanges; *d*, processes; *e*, Boll's line.

longitudinal section the cells appear rectangular, and in transverse, stellate—the anastomosing processes being sections of the plates. *Boll's stripe* or *line*, seen in teased preparations, is due to a lateral

plate being seen in face view. Each plate at its periphery breaks up into a fringe of delicate protoplasmic processes which anastomose with corresponding processes from cells between adjacent bundles. Both the cells and their processes can be clearly revealed by gold chloride, which gives the "positive" of the "negative" produced by silver nitrate. The nuclei of adjacent cells in the same series or row lie at their contiguous ends. (*c*) In the *ligamenta subflava* the elastic fibres predominate. They are larger than those of areolar tissue. The white fibrous element surrounds the ligament and penetrates between the bundles of elastic fibres.

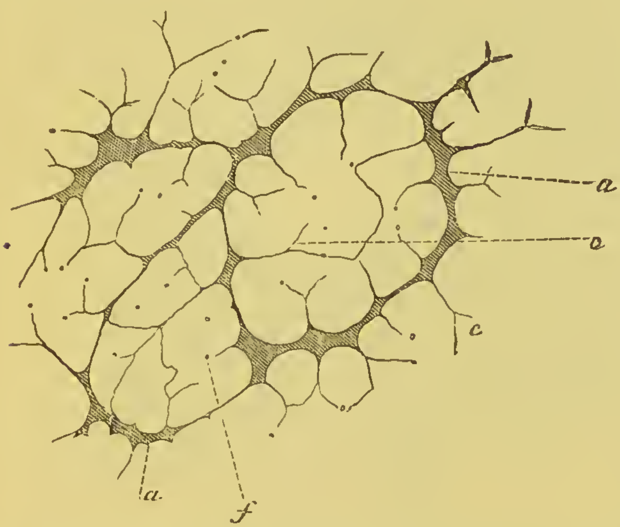


Fig. 43.—Transverse Section of Tendon of Tail of Young Rat (×400).

a, Boundary of a bundle of connective tissue; *c*, lateral expansions of neighbouring cells anastomosing; *f*, elastic fibres lying amongst the white between the cells, cut transversely.

Fig. 44.—From the Tendon of the Tail of a Young Rat, showing a Row of Tendon Cells and Bundles of White Fibres (×500).

c, Tendon cell; *f*, white fibres; *e*, a "flange," in face view.

Development of connective tissue.—There have long been two theories—(1) *That the fibres are produced by a transformation of the cell substance.* In favour of this view the cells in growing areolar tissue often appear to be lying upon a fibre, as if the latter had been produced by fibrillation of part of the substance of the cell, the latter maintaining its original size by compensatory growth; (2) *that the fibres appear in the matrix,*

perhaps under the influence of the cells, but unassociated with any transformation of their protoplasm. In the development of elastic cartilage (arytenoid of ox or sheep) the elastic fibres appear in the matrix entirely unconnected with the cells in any way. The same takes place in embryonic mucous tissue—as the umbilical cord becomes partially converted to fibrous tissue towards the end of intra-uterine life, fibres appear in the mucinous matrix quite apart from the cells.

Fig. 45.—Internal Lamella from the Lamellated Sheath of the Pneumogastric Nerve of Dog, to show the Development of Elastic Tissue by the Deposition of Fine Granules of Elastin (× 400).

P, Elastic plate formed by the fusion of elastin granules; *g*, elastin granule; *r*, fibre formed of small granules of elastin in series; *fc*, connective tissue fibres.

In the case of bone, hyaline cartilage, and dentine, the production of the fibrillated matrix undoubtedly appears to be due to a process similar to that of secretion on the part of the cells themselves, and it may be that the white fibres of connective tissue are produced in this way. In elastic cartilage, however, it must be admitted that the analogy to secretion is not so clear, the cells not being in immediate contact with the fibrils.

3. **Adipose tissue** is developed in young connective tissue by a transformation of its cells to fat cells. A fat cell consists of a membrane enclosing a globule of oil, and a flattened nucleus at one side between the two. A little protoplasm may surround the nucleus, and the cell often thus presents somewhat the appearance of a signet ring. The cells are supported by delicate connective

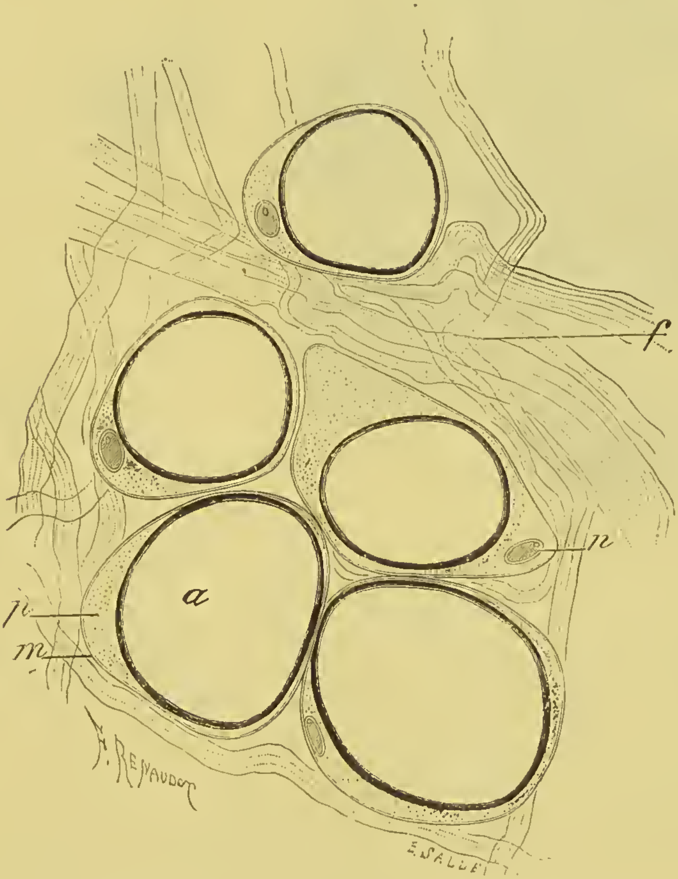


Fig. 46.—Fat Cells in Subcutaneous Tissue of Dog (×200).
a, Oil globule; *p*, protoplasm; *n*, nucleus; *m*, cell membrane; *f*, white fibres.

tissue, and are grouped together to form lobules, and these again to form lobes. Each lobule has an afferent artery, and one or more efferent veins, with an elaborate capillary plexus between them, in the meshes of which lie the individual cells.

A vertical section of the subcutaneous tissue of a young animal, in which fat is being developed, may be stained with osmic acid and studied for development of fat cells. The young

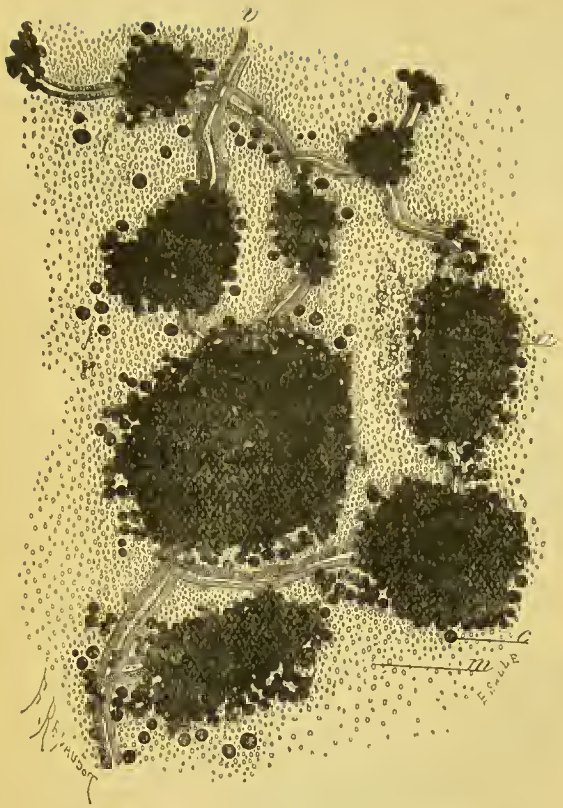


Fig. 47.—Subcutaneous Tissue of Embryo Ox, stained with Osmic Acid (×50).

a, Fat lobule; *c*, isolated fat cell at the periphery of a lobule; *m*, embryonic connective tissue; *v*. blood-vessel.

Fig. 48.—Developing Fat Cells from Subcutaneous Tissue of Embryo Ox, stained with Osmic Acid (×550).

a, Fat cell almost completely developed; *n*, nucleus; *g*, fat granules in the protoplasm surrounding the nucleus; *d*, fat cell in early stage of development; *b* and *c*, fat cells at intermediate stages.

connective tissue corpuscles become studded with two, three, or more droplets of fat (stained black), and these increase in size and run together to form one large drop. Thus a direct transformation of the protoplasm of the cell to fat takes place, the cell becoming enlarged and globular, and its nucleus being pushed to one side. (For chemistry of fat, see page 18).

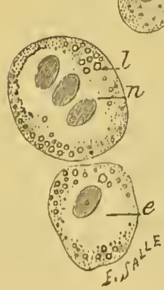


Fig. 49.—Fat Cells of Mesentery of newly-born Rat.

n, Nucleus; *p*, protoplasm; *l*, fat droplets; *e*, protoplasm immediately around the nucleus, free from fat droplets.

4. **Adenoid tissue** is found in the spleen, thymus, and lymphatic glands. It is also found in the mucosa and submucosa of the alimentary tract, where it forms solitary follicles or Peyer's patches. It consists of a delicate fibrillated network covered by nucleated branching cells, the nucleated body of a cell lying upon a node, and the branches extending along the strands of the network passing from it. The fibrillated nature of the latter is not therefore apparent unless the cells are first artificially removed. All the mucin has disappeared from the meshes of the network, which contain instead a large number of lymph cells—small round cells with a single nucleus and little perinuclear protoplasm. They may be present to such an extent as to entirely conceal the adenoid reticulum, as in the lymph follicles of a lymphatic gland; but in the lymph sinus surrounding the follicles, where the network is coarser and there are fewer lymph cells, the network can be easily made out, especially if the lymph corpuscles are removed by washing. The branching cells correspond to the ordinary connective tissue cells, the fibrillated network to the white fibres, and the lymph corpuscles to the wandering cells. The mucinous matrix has disappeared.

Fig. 50.—Adenoid Tissue of Human Lymphatic Gland.

a, Branched corpuscles; *b*, network; *c*, leucocytes.

5. **Neuroglia.**—This is the name given to the form of connective tissue found in the grey and white matter of the central nervous system. It is to be noted that it is of epiblastic origin, being developed in connection with the cells lining the central canal. It consists of large nucleated cells, which, by their numerous branching processes, anastomose with each other and with the strands of connective tissue sent in from the pia mater, and form a very delicate interlacement for the support of the nerve elements.

6. **Cartilage.**—Of this there are three varieties—hyaline, white fibro-cartilage, and yellow elastic cartilage. (1) *Hyaline cartilage* covers the articular ends of long bones, and constitutes the costal

Fig. 51.—Cartilage of the Head of the Femur of Frog (×600).
s, Ground substance; *c*, capsule; *n*, nucleus; *n'*, nucleolus.

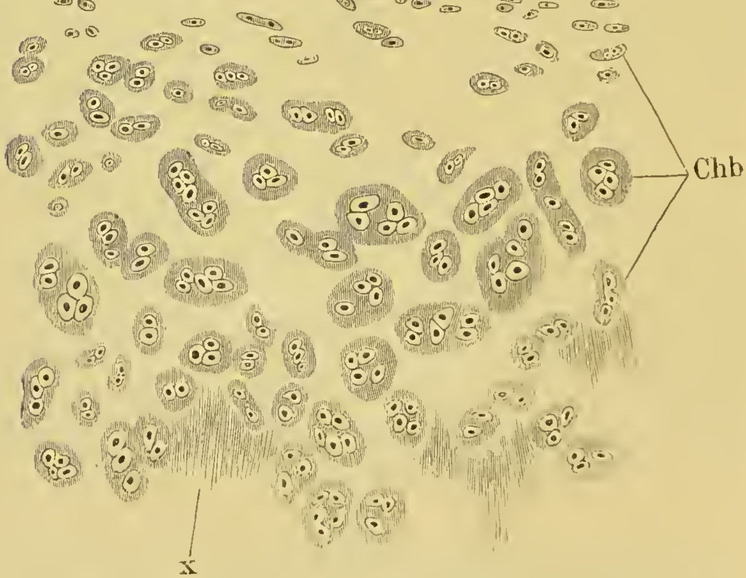


Fig. 52.—Hyaline Cartilage. Transverse Section of Human Thyroid.
x. Fibrous matrix; Chb. Cartilage-capsules; Pch. Perichondrium.

cartilages and those of the nose, larynx, trachea and bronchi, with the exception of the epiglottis and cornicula laryngis. Its cells are surrounded by capsules and embedded in a hyaline or ground-glass matrix. This is formed in the first place from the coalescence of previously-formed capsules; it is fibrillated like white fibrous tissue, and, like it, the fibrils are cemented together by a mucinous ground substance which reduces nitrate of silver. In old age the fibrillation is more marked, a deposit of calcareous salts occurring between the fibrils.

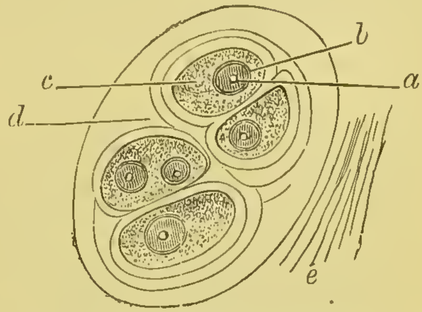


Fig. 53.—Cartilage Cells from Calcaneum of Embryo Dog, from the neighbourhood of the Line of Ossification.

d, Primary and secondary capsules; *c*, cell protoplasm; *b*, nucleus; *a*, nucleolus; *e*, fibrous matrix.

In costal cartilage the cartilage itself is seen to be invested by a fibrous perichondrium, between which and the cartilage immediately beneath it no very distinct line can be drawn. The cells at the periphery of the cartilage are flattened in the plane of its surface, and in section resemble the fusiform cells of the perichondrium. More deeply, they are round or oval, irregularly placed, and a capsule is easily distinguishable. They are frequently in pairs or fours, the original cell having divided into two daughter cells, each of which secretes a new capsule, that of the parent cell presently fusing with the surrounding matrix; and the same process of division may be repeated, accompanied with the production of fresh capsules, until the group may number a dozen cells or more. But the matrix is also produced in another and more important way after the early embryonic stage of cartilage formation is passed. The deeper part of the

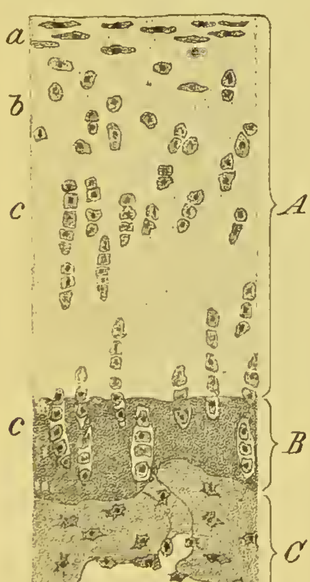


Fig. 54.—Articular Cartilage of Dog (× 200).

A, Hyaline cartilage; *B*, hyaline cartilage calcified; *C*, bone; *a*, flattened cells near surface of cartilage; *b*, more deeply placed rounded cells; *c*, cells arranged in vertical rows.

perichondrium undergoes transformation to cartilage, its fibres becoming hyaline matrix and its connective tissue corpuscles cartilage cells, while this is compensated for by the growth of the perichondrium peripherally. It is thus that the costal cartilages increase in thickness during adolescence. (*Cf.* periosteal growth of bone.)

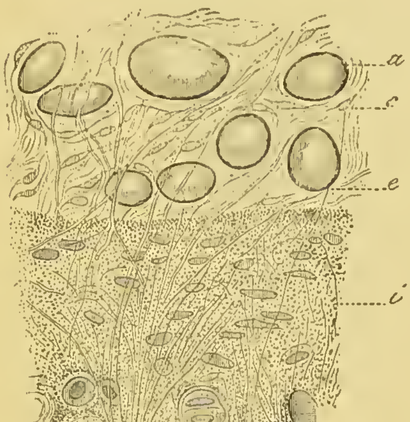


Fig. 55.—Transverse Section of Epiglottis of Dog (×170).

a, Fat cells; *c*, connective tissue; *e*, elastic fibres; *i*, superficial layers of cartilage with small cells; *r*, central cartilage with larger cells in capsules, *l*, and a ground substance composed of fibres and granules of elastin; *f*, bundles of connective tissue cut transversely.

In articular cartilage the cells are arranged in vertical rows, except at the surface, where they are flattened, and with which they are in the same plane. A layer of calcified cartilage matrix is found immediately next to the bone when the animal has attained some age. In costal cartilage the fibrils of the matrix run parallel with the surface; in articular, vertical to it. (2) *White fibro-cartilage* forms the intervertebral discs and the menisci of joints. It deepens the cavities of the hip and shoulder joints, and lines the grooves on the surface of bones for tendons. It forms the semilunar cartilages of the knee. It is nearly allied to ordinary connective tissue. The intervertebral discs in their outer parts are formed of layers of dense white fibrous tissue, in which are found branching connective tissue cells. Towards the centre of the disc the cells take on the characters of cartilage cells, becoming oval or round, and exhibiting a distinct hyaline capsule. Sometimes they are laminated concentrically, like a grain of starch, from the formation of successive cartilage capsules. Branching processes may sometimes be seen passing from one cell to anastomose with similar ones from its

neighbours. (3) *Yellow elastic cartilage* is found in the epiglottis, the cornicula laryngis, the ear, and the Eustachian tube. It consists of a dense feltwork of elastic fibres, in which are placed cartilage cells surrounded with a distinct hyaline capsule.

If the arytenoid cartilage of an ox be examined, as we pass from the purely hyaline portion to the elastic area, fibres of

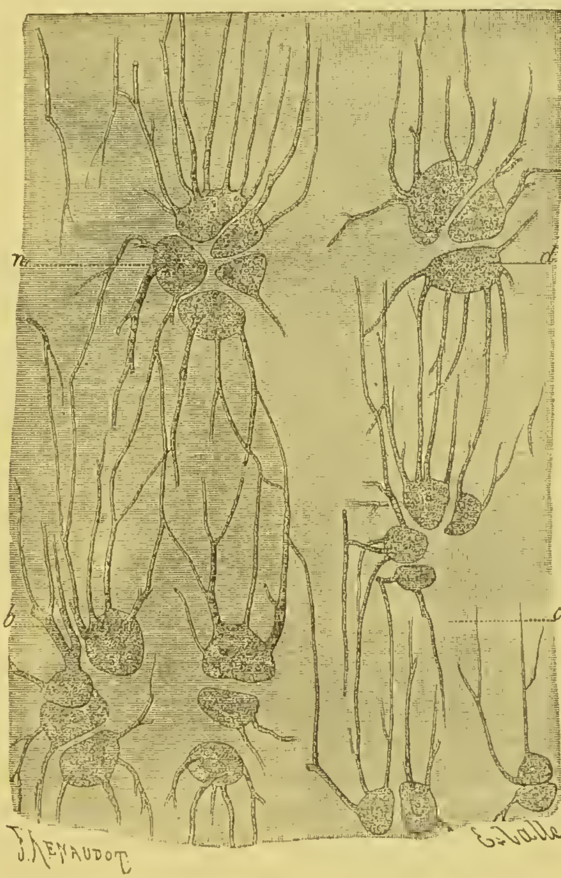


Fig. 56.—Cartilage of Cuttlefish.

c, Matrix; *d*, cartilage cells; *b*, *n*, anastomosing processes of cells.

elastin first appear here and there in the hyaline matrix, entirely separate from the cells, and isolated from each other; then in increasing number, and as the elastic portion is reached, they form a dense feltwork, the hyaline matrix only remaining visible in the form of pericellular capsules. All the three forms of cartilage are extra-vascular, and, it may be, are nourished by the percolation

of lymph through delicate channels between the cell spaces. Such channels are evident in the hyaline cartilage of the squid and cuttlefish (Fig. 56), but have not been clearly demonstrated in human hyaline cartilage.

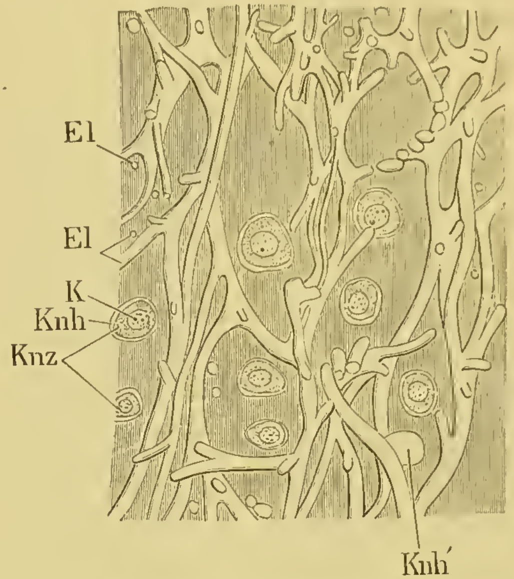


Fig. 57.—Elastic Cartilage of Ear of Horse.

El, Elastic fibres cut in various directions; K, Nucleus of cartilage-cell; Knh. contour of cartilage-cell cavity; Knh′, empty cartilage capsule; Knz, cartilage-cell.

7. **Bone** is of two varieties—the *compact* and the *cancellous*. Compact bone is found forming the shaft of long bones, except that part immediately surrounding the medullary cavity, the shell of the short and cuboidal bones of the hand and foot, and that of the irregular bones of the head and the tables of the flat bones of the skull. Cancellous bone surrounds the medullary cavity of long bones, and forms the mass of their lighter spongy ends, and of the short or cuboidal bones of the hand and foot, the irregular bones, the inner part of the clavicle and ribs, and the diploe of the flat bones of the skull.

Bone, whether compact or cancellated, consists of *cells*, lying in cell spaces, embedded in a *calcified fibrous matrix*, traversed by a system of vascular channels—the *Haversian canals*—containing blood-vessels, lymphatics, and nerves. If subjected to the action of mineral acid the calcareous matter may be removed, and a long bone so treated may be tied in a knot, regaining its original form to a large extent when released. But if subjected to calcination,

on the other hand, the organic fibrous part is removed and only a brittle calcareous simulacrum of the original bone is left.

Bone is covered by a fibrous investment—the periosteum—and the medullary spaces and cancelli are filled with marrow. The structure may readily be studied in unsoftened and softened sections of a long bone.

The *matrix* is arranged in the form of lamellæ. In structure a lamella consists of a series of fibrils running parallel with each other and in the same plane; the fibrils of one lamella, however, usually run at an angle to those of its neighbours. The lamellæ are probably of the nature of white fibrous tissue, and have undergone calcification. In the shaft of a long bone four systems of them are readily discernible — (1) The peripheric, which occur in considerable number immediately beneath the periosteum, each surrounding the bone to a greater or less extent. (2) The perimedullary, surrounding the medullary canal, as their name implies. (3) Haversian lamellæ, surrounding the Haversian canals, which have been already referred to as containing blood-vessels, lymphatics, and nerves. These canals in the shaft of a long bone form a system of tubes running longitudinally, and intercommunicating with each other by anastomosing lateral channels, and also, on the one hand, with the surface of the bone, and on the other with the medullary cavity. Many lamellæ surround each canal, forming

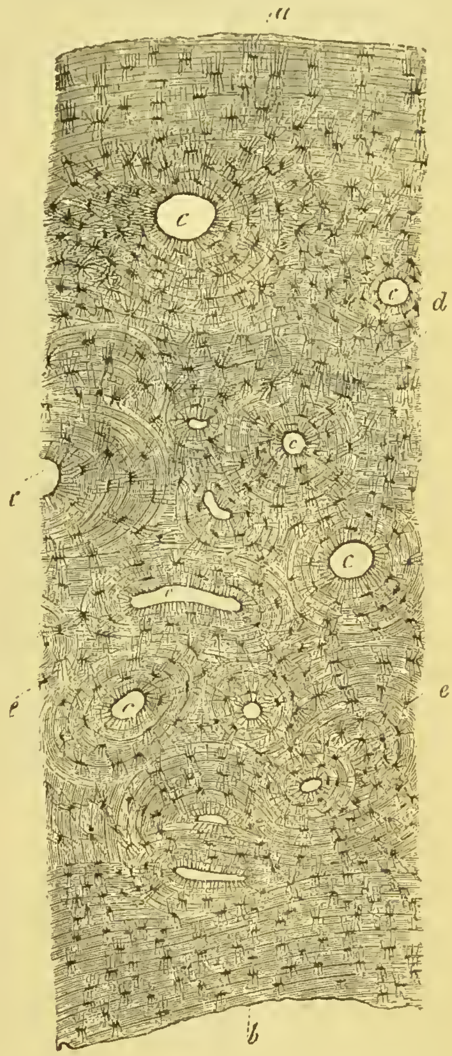


Fig. 58.—Transverse Section of Shaft of Metacarpal Bones of Man.

a, Peripheral lamellæ; *b*, perimedullary lamellæ; *c*, Haversian canals surrounded by their lamellæ; *d*, intermediate systems of lamellæ; *e*, bone corpuscles.

with the canal contents an *Haversian system*, the lamellæ being optically distinguishable from each other under the microscope by the different way in which the fibrils forming them are cut. Thus the fibrils of one lamella may be cut transversely, while those of the lamella adjacent are cut longitudinally. These Haversian systems are thus formed of a number of tubes, one within the other. (4) The intermediate lamellæ lie between the Haversian systems within the peripheric system, and outside the perimedullary.

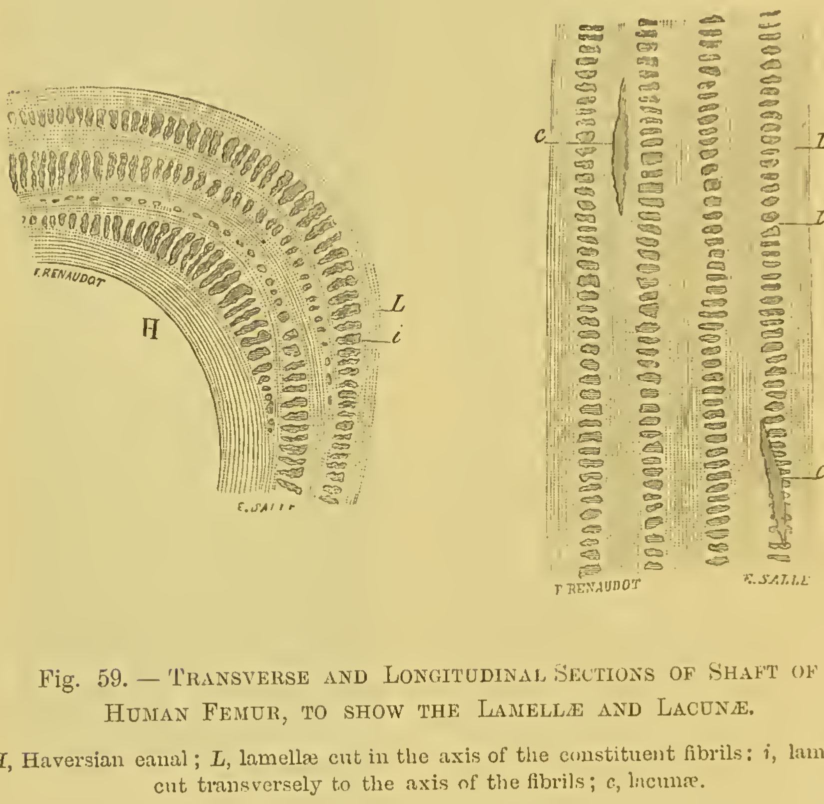


Fig. 59. — Transverse and Longitudinal Sections of Shaft of Human Femur, to show the Lamellæ and Lacunæ.

H, Haversian canal; *L*, lamellæ cut in the axis of the constituent fibrils: *i*, lamellæ cut transversely to the axis of the fibrils; *c*, lacunæ.

They do not belong to any of the three divisions already named, but lie intermediate to the Haversian systems, upon which they often directly abut, their plane being at an angle—it may be a right angle—to that of the lamellæ of the Haversian systems. They are the remains of previous Haversian systems, which have been partially destroyed to make way for new ones, and often of portions of the peripheric system which have been involved in the process of removal and reconstruction from within during the growth of the bone (see "Development of Bone").

But in addition to the calcified fibrous matrix represented by these lamellæ, certain fibres — *Sharpey's* or *perforating* fibres— are found. These are originally derived from the periosteum, and are of the nature of white, or more rarely of yellow, elastic fibres. They have been included from the periosteum in the formation of the peripheric lamellæ. They are calcified, and serve to bind the lamellæ, which they pierce, together, much in the same way

Fig. 60. — Transverse Section of Shaft of Femur of Man (× 300).

H, Haversian canal; *c*, lacuna for bone corpuscles; *a*, lacuna at periphery of Haversian system showing recurrent canaliculi; *s*, intermediate system of lamellæ with fibres of Sharpey (*h*) cut transversely; *p*, large fibres of Sharpey of the intermediate systems.

as a nail does superimposed boards of wood through which it is driven.

They are not found, however, in the Haversian systems, at the outer edge of which they stop short suddenly (see " Development of Bone").

The *cells* corresponding to the fixed corpuscles of connective tissue are nucleated, branched, and flattened, conformably with the

space between the lamellæ in which they lie, appearing fusiform on section. Their branches communicate through the lamellæ with those of cells in adjacent planes. The cell spaces themselves are termed *lacunæ*, and the delicate channels in which their branches lie the *canaliculi*. By this system of cell spaces with inter-communicating channels the permeation of the bone substance by lymph is secured. The lacunæ immediately surrounding an Haversian canal open into it by their canaliculi, and the lacunæ at the periphery of a system may communicate with the canaliculi of lacunæ at the periphery of neighbouring systems; but more usually the canaliculi turn back into their own systems, and are hence named "recurrent." The canaliculi at the surface of the bone open into the periosteum, and those most internal into the medullary cavity. The cells and their processes are said to be surrounded by a delicate elastic membrane lining the spaces in which they lie. The *periosteum* of the bone consists of an outer fibrous covering and an inner loose layer, which in growing bone is termed the osteogenetic layer, as it contains the osteoblasts which secrete the matrix. It passes into the Haversian canals, carrying with it blood-vessels, lymphatics, and nerves, which traverse the bone and communicate with the contents of the medullary cavity. The *medullary cavity* contains yellow marrow, and is immediately bounded by bone of a more open cancellous nature than that of the heavier compact part of the shaft, the cancellous spaces communicating, on the one hand, with the Haversian canals of the compact shaft, and on the other with the central space. *Yellow marrow* consists for the most part

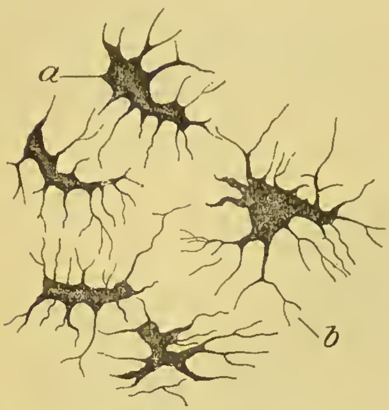


Fig. 61.—Bone Lacunæ and Canaliculi from Section of Carapace of Tortoise (× 350).

a, Lacuna; *b*, canaliculi.

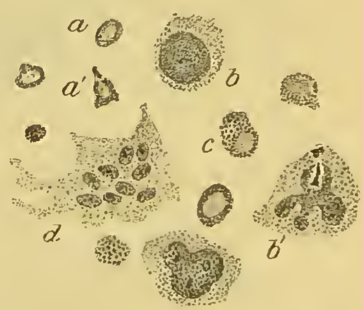


Fig. 62.—Cover-glass Preparation of Marrow from Bone of Rabbit (× 200).

a, Small marrow cell; *a′*, small marrow cell budding; *b*, large marrow cell; *b′*, large marrow cell with dividing nucleus; *c*, cell containing reddish granules; *d*, myeloplax.

of fat cells, blood-vessels, and connective tissue, and is found in the medullary canal of long bones and the larger cancelli.

As opposed to the shaft, the end of a long bone, except the shell, is *cancellous*, and has no central canal. The thin hard outer shell of compact bone encloses an internal spongy cancellous tissue, the cancelli being filled with *red marrow*. This consists of a system of large intercommunicating venous channels with thin walls, into which the terminal divisions of the afferent artery directly open, supported by delicate connective tissue, a few fat cells, and marrow cells in large quantity, of which there are several varieties. (1) Marrow cells proper, which resemble leucocytes, but are somewhat larger. They are mono-nucleated, amœboid, and occasionally exhibit coloured granules in their peri-nuclear protoplasm. (2) Erythroblasts, which are smaller, coloured, nucleated, and are probably descendants of the coloured nucleated cells of the embryo. (3) Myeloplaxes, which are large, multi-nucleated, irregular cells, probably connected with the removal of bone. Smaller cells than these, probably the same in process of development, exhibit a single nucleus with indications of impending division; or this may have gone far enough for sub-division to have taken place, the separate portions being then united, however, by a thread of nuclear substance.

Development of Bone.—All the bones of the body, with the exception of the flat bones of the skull and the irregular bones of the face, are preceded in the embryo by a cartilaginous simulacrum, in and around which bone formation takes place. The tables of the skull and the bones of the face, on the other hand, are preformed in membrane. Thus, ossification is said to be either *intra-cartilaginous* or *intra-membranous*. But it is to be borne in mind that even when a cartilaginous rod precedes the ultimate bone it takes no real part in its formation, but is only the scaffolding, so to speak, upon which the permanent bone is built up. All permanent bone is developed in membrane.

Intra-cartilaginous development of Bone.—In a long bone, such as the tibia or femur, the process of ossification begins in the centre, and it may be divided into four stages.

1. *Proliferation.*—The cells in the centre of the cartilaginous rod increase in size and proliferate, each daughter cell at first

secreting around it a cartilage capsule. But division goes on so quickly that separate capsules cease to be formed, and the cells now come to lie in groups in spaces which are called the *primary areolæ*. In the meantime the cartilage cells above and below the centre of ossification have also been dividing in the direction of the long axis of the shaft, and now extend in vertical rows towards the ends of the bone.

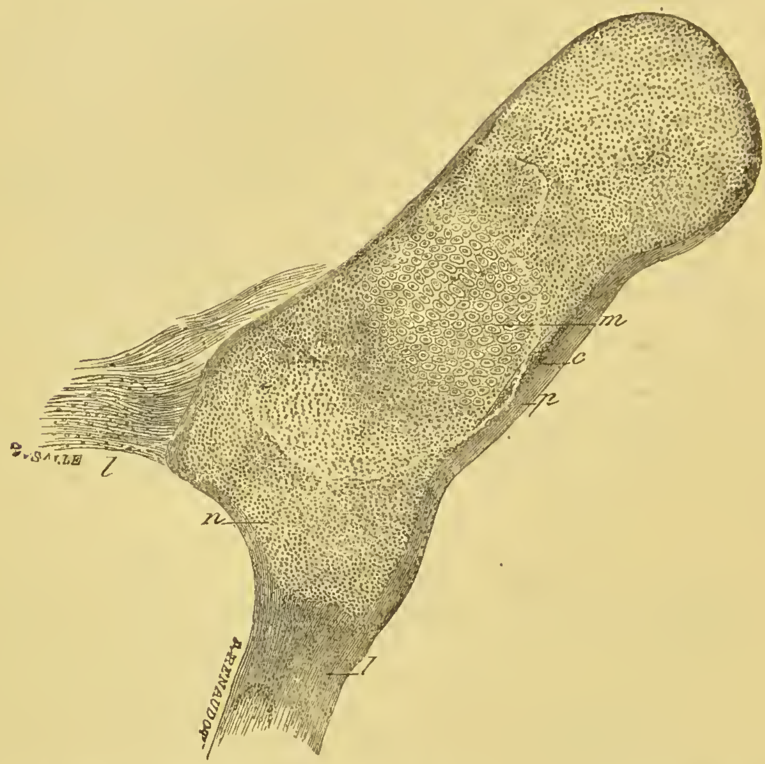


Fig. 63.—LONGITUDINAL SECTION OF METACARPAL BONE OF EMBRYO DOG (×43).

m, Central proliferating cartilage cells; *c*, layer of perichondrial (subperiosteal) bone; *p*, perichondrium or periosteum; *n*, cartilage of head of bone; *l*, tendinous attachments.

2. *Calcification.*—The cartilage separating the primary areolæ now undergoes calcification, and the process extends to that separating the vertical rows of cells. At this time also it may be noted in passing that subperiostal formation of the bone commences (see below).

3. *Vascularisation,* characterised by an irruption of blood-vessels and connective tissue from the deeper layer of the

periosteum, now sets in. The advancing blood capillary loops dissolve the cartilage before them and open into the primary areolæ, which they bring into communication with each other, and thus give rise to what are known as the *secondary areolæ* or *secondary areolar spaces.* But they go further than this, and turning towards the two ends of the shaft, advance in the lines of the vertical rows of cartilage cells, dissolving both cartilage and cells as they go, and leaving only calcified cartilage trabeculæ between the rows.

4. *Ossification.*—The advancing blood-vessels are accompanied by delicate connective tissue, the cells of which now take on a new function, that of *osteoblasts*, and proceed to lay down bone upon the remains of the calcified cartilage separating the areolar spaces, and on the sides of the cartilage trabeculæ which separated the vertical rows of cells. Inasmuch as the process commences in the centre of the bone and extends towards the ends, the layer now laid down is thicker in the centre, and thins out as it approaches the "line of progression" of the advancing vascular loops.

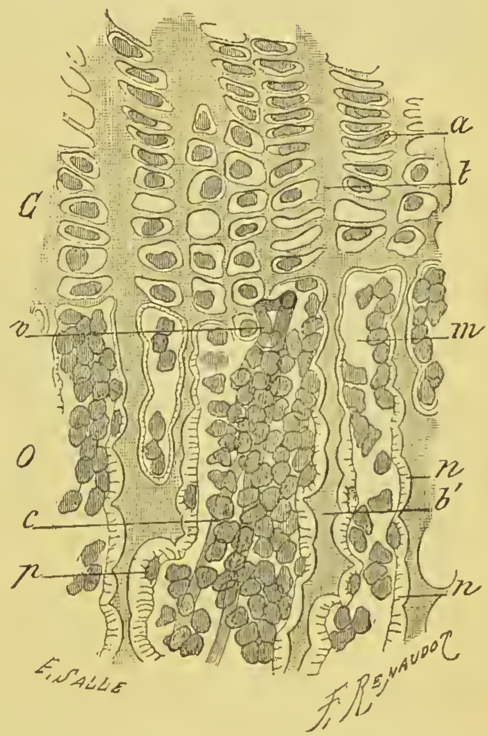


Fig. 64.—Longitudinal Section of Head of Metacarpal Bone of Young Rabbit (×240).

C, Cartilage; *O*, bone; *a*, cartilage cell; *b*, cartilage trabecula; *m*, medullary space; *n*, layer of bone; *b′*, trabecula on which bone is being laid down; *p*, bone-corpuscle; *c*, medullary cells; *v*, blood-vessel.

The osteoblasts, as above stated, are modified connective tissue cells, which take on their new function after the entrance of the blood-vessels which they accompany. The bone is laid down upon the cartilaginous trabeculæ as follows:—An osteoblast lying on the surface of the cartilage, by a process of solution comparable to digestion, produces a small hollow or bay in the cartilage, and secretes around it true bone. As it does so it acquires processes, and remains *in situ* as a true

bone-corpuscle. But although the bone laid down upon the cartilage trabeculæ is true bony matrix, and contains real bone-corpuscles, it is merely of a temporary nature, and is all removed during the process of further growth to make way for the central medullary canal. The processes of construction and removal can indeed be seen going on side by side. Certain large multi-nucleated cells, called *osteoclasts* (which are either modified connective tissue cells or the surviving cartilage cells), may be seen in places attached either to the sides or ends of the calcified cartilage trabeculæ, which, with the bone laid down upon them, they are removing. These cells, as we shall see, are also to be found on the surface of the bone beneath the periosteum, especially where "modelling" is going on to any great extent, as in the irregular bones of the skull.

While this is going on the bone steadily increases in length, and this is effected by the persistence of what may be termed a "cambium" layer of cartilage. Immediately beyond the line of progression—the line of the advancing vascular loops with their accompanying osteoblasts — the cartilage cells continue to divide in the axis of the shaft, so that the conversion to temporary bone on the one side of the line is compensated for by continued growth of the cartilage on the other.

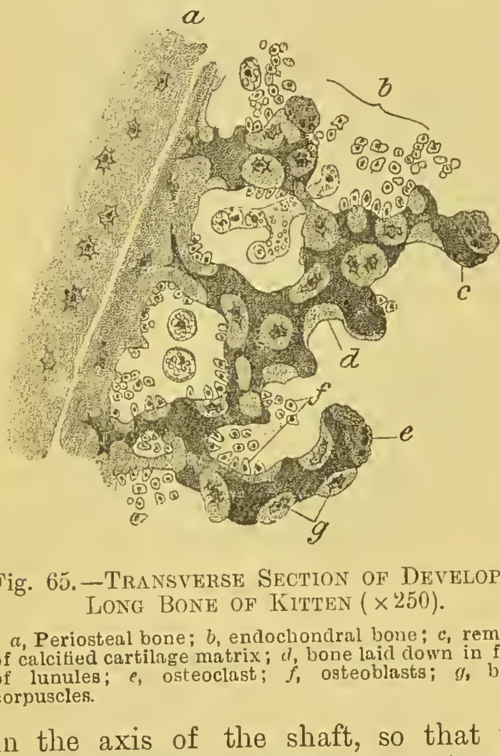


Fig. 65.—Transverse Section of Developing Long Bone of Kitten (×250).

a, Periosteal bone; *b*, endochondral bone; *c*, remains of calcified cartilage matrix; *d*, bone laid down in form of lunules; *e*, osteoclast; *f*, osteoblasts; *g*, bone-corpuscles.

The ossification of the epiphysis starts at a later date to that of the shaft, but proceeds in much the same way, except that there is no medullary canal to be formed, but merely cancellous spaces. As long as the bone continues to grow in length, the layer of proliferating cartilage cells remains between the epiphysis and diaphysis. Ultimately it disappears, and in old age the epiphyses are joined to the shaft by a bony union. In this way the age of the individual may be roughly estimated. In early life the

epiphyses are readily separable from the shaft, either before or after maceration.

Periosteal bone formation, as already stated, starts about the same time as calcification and the irruption of the vascular loops. The periosteum at this time consists of two layers—a superficial, composed of lamellæ of white fibrous tissue, with flattened connective tissue cells between them; and a deeper, looser, *osteogenetic* layer of more delicate connective tissue and many young osteogenetic cells or osteoblasts. Both layers contain blood-vessels, lymphatics, and nerves. The first step in periosteal bone formation consists in a direct conversion of the inner part of the deeper layer to bone. The white fibres undergo calcification by the deposition of calcareous salts between the fibrils forming them, and the cells assume the functions of osteoblasts, and secrete bone upon the fibres and around themselves, becoming branched as they do so, and assuming the characteristics of true bone-corpuscles. In this way a thin layer of bone outside the cartilaginous simulacrum is produced, which increases in thickness, and the further history of periosteal bone formation consists in the compensatory growth of the deep layer of periosteum on its outer side as it is converted to bone on the inner; the process of ossification thus progressively extending outwards as the bone grows in thickness, while this is accompanied (when the cartilaginous bone has been removed) by removal from the inside by osteoblasts to secure the enlarged medullary canal of the growing bone.

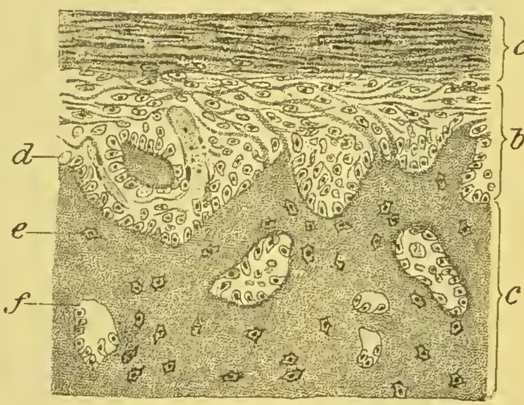


Fig. 66.—Transverse Section of Developing Bone of Kitten to show Periosteal Bone Formation (×200).

a, Outer fibrous layer of periosteum; *b*, inner cellular layer of periosteum; *c*, bone; *d*, layer of osteoblasts; *e*, bone-corpuscle; *f*, Haversian space.

Here and there at the surface beneath the periosteum large multinucleated cells, or osteoclasts, may be seen engaged in modelling the outer contour, especially in the case of the irregular bones. They lie in little pits or hollows, termed *Howship's foveoli*, produced by their solution of the bony matrix.

The Haversian canals and spaces are formed as follows:— At the surface of the bone, especially in transverse sections, there will frequently be seen an appearance of two "flying buttresses," projecting towards each other and about to enclose a space. This space indicates the position of a future Haversian canal, and contains delicate connective tissue and osteoblasts derived from the periosteum. Before its conversion to an Haversian system the space becomes enlarged at the expense of the peripheric lamellæ, and this enlargement is succeeded by a deposition of new bone in concentric lamellæ to form the layers of the Haversian system. This process of enlargement, followed by reconstruction in the Haversian system, continues throughout life, as the older bone is constantly being replaced by new. It will be understood from this why Sharpey's fibres are found in the peripheric lamellæ and their remains only. They are included from the periosteum as the peripheric lamellæ are laid down. As these latter are removed in part during the enlargement of an Haversian space, the fibres are naturally removed with them, and thus abruptly terminate at the outer edge of the Haversian system.

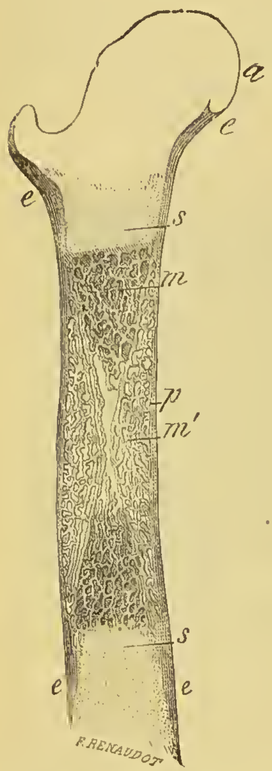


Fig. 67.—Longitudinal Section of Humerus of Embryo Dog (×7).

a, Cartilaginous head of bone; *m*, cartilaginous bone; *m'*, periosteal bone; *s*, cartilage cells in vertical rows; *p*, periosteum; *e*, perichondrium or continuation of periosteum fusing with hyaline cartilage of head of bone.

Intra-membranous Ossification.—The vault of the skull, the irregular bones of the face and the lower jaw are preformed in membrane. The lower jaw is represented in early embryonic life by Meckel's cartilage, but this takes no part, even as a scaffolding, in the formation of the future bone, which is formed in membrane round it. Such a bone as the parietal consists at first of a delicate sheet of white fibrous tissue, and ossification starts about its centre. It is precisely comparable to periosteal bone formation. The fibres at the point of ossification undergo calcification, and the corpuscles assume the function of osteoblasts, and lay down bone upon them and around

themselves. The network of blood-vessels in the connective tissue marks out the path of the primary Haversian canals. The process of ossification extends from the central point towards the edges of the bone, where, however, a fringe of growing connective tissue always persists as long as the bone has to grow—a "cambium" layer comparable to the cartilage beyond the "line of progression" in the long bone already described. This growing edge provides for the extension of the bone laterally, which is increased in thickness by a deposition of bone by the periosteum covering its

Fig. 68.—Vertical Section of Cranial Bone of Fœtal Mouse (Intra-Membranous Ossification) (×300).

a, Fibrous layer of periosteum; *b*, growing osteogenetic layer of periosteum; *c*, calcified fibrous tissue; *d*, osteoblasts; *e*, capillary blood-vessels.

surface, the diploe being opened up at the same time by osteoclasts, and the cancelli of the adult bone formed. In old age the cambium edge disappears, and true bony union of the plates of the vault of the skull may take place.

8. **Dentine.**—Though only a part of a tooth is composed of dentine, it will be convenient to consider the whole structure and

development here. A tooth consists of two parts—the *crown* and the *fang ;* the *neck*, at the level of the gum, marks the point of junction between the two. The crown varies in shape according as the tooth is a cutting or grinding one—an incisor or a molar. The fang is sometimes single, sometimes double, tripartite, or may show four subdivisions. The crown is covered with *enamel*, and the fang with *crusta petrosa*. The tooth is hollowed out inside to form the *pulp cavity*, which extends into the crown and each fang, at the lower extremity of which it opens to admit the nerve fibres and blood-vessels from the dental canal. By far the greater part of the tooth is composed of *dentine*, which consists of a series of delicate-branched tubules embedded in a calcified homogeneous matrix. The dentinal tubules lie side by side, and give to the dentine a striated appearance. They are probably of the nature of elastin, and divide dichotomously as they proceed from the pulp cavity outwards. The direction of the tubules varies according to the part of the tooth in which they occur. In the fang they pass horizontally outwards, and at the summit of the crown vertically, and in the intermediate part of the crown the direction is intermediate. At the periphery of the dentinal matrix are found a number of *interglobular spaces*, a series of small spaces whose contour is made up of a number of convexities inwards, and which appear black from the air they contain. They result from imperfect calcification of the matrix. The growth of the dentine, or rather the stages of its calcification, are marked by certain *incremental lines*, which run in the same plane as its surfaces. The dentinal tubules contain the dentinal fibres, which are the terminal processes of the odontoblasts, and

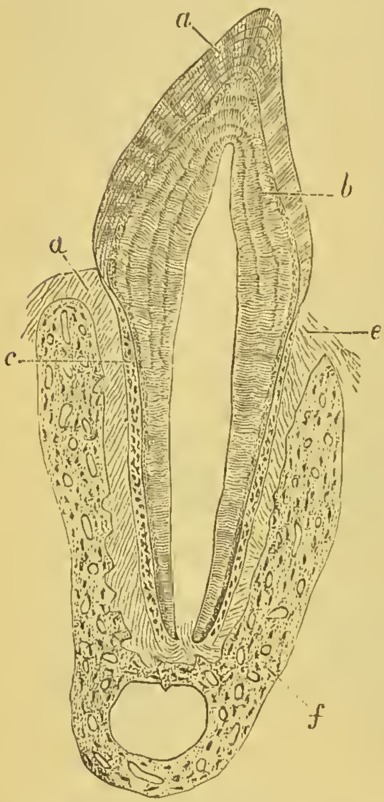


Fig. 69. — Longitudinal Section through a Premolar Tooth of Cat.

a, Enamel ; *b*, dentine ; *c*, crusta petrosa ; *d* and *e*, periosteum ; *f*, bone of alveolus.

thus of the dental nerves. It is these fibres that convey the sensation of pain when a carious tooth is scraped. The crusta petrosa forms a thin covering to the fang of the tooth, ceasing at its neck. It consists of bone, characterised by an absence of Haversian systems. The enamel covering the crown is the hardest tissue in the body, and is formed almost entirely of calcium salts deposited in the form of hexagonal prisms placed vertically to the surface they cover, the hexagonal outline representing that of the original cells from which the enamel is developed. In vertical section the enamel prisms show transverse markings, and are frequently somewhat wavy in their course.

The alveolus of the jaw is hollowed out to accommodate the teeth; but uniting the two, and also acting as a buffer between their hard and resisting surfaces, is found the *periodontal membrane.* This is composed of ordinary connective tissue, strengthened by transverse fibres, passing on one side into the bone of the alveolus, and on the other into the crusta petrosa of the fang. It is, in fact, the periosteum of the

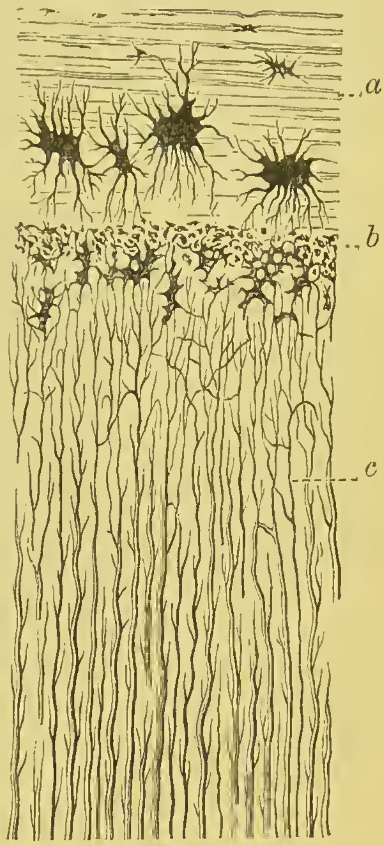


Fig. 70.—From a Section through a Canine Tooth of Man.

a, Crusta petrosa with large bone-corpuscles; *b*, inter-globular spaces; *c*, dentinal tubules.

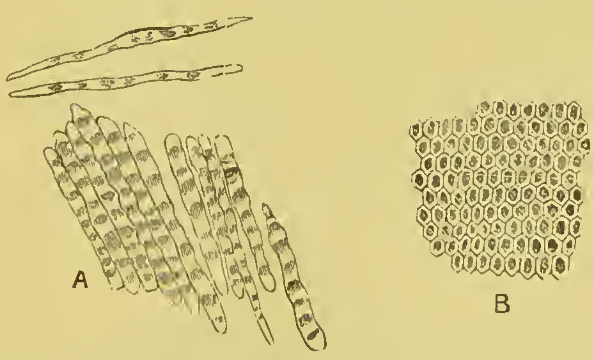


Fig. 71.—Enamel Prisms.
A, In longitudinal view; *B*, in cross section.

jaw, and the transverse fibres are comparable to Sharpey's. If it be traced upwards it will be found to be continuous with the connective tissue beneath the epithelium of the gum around the neck of the tooth, while below it will be found in continuity with the connective tissue of the dental canal and the pulp cavity. This latter contains delicate connective tissue supporting the terminations of the dental blood-vessels and nerves. The peripheral cells of the pulp tissue—those next to the dentine—have developed into odontoblasts, somewhat columnar-shaped nucleated cells connected by their pointed inner extremities with terminal nerve fibrils. The broad end of the cell is applied to the dentine, and from it proceeds the delicate process occupying a dentinal tubule. The dental canal extends through the length of the alveolus, and forms a tubular space in the bone below the level of the periodontal membrane. It contains connective tissue, blood-vessels, and the branches of the dental nerve, and is patent above at intervals to give passage to these on their way to the pulp cavity.

Development of the Teeth.—The teeth are developed in two series—(1) the *temporary*, which give way to (2) the *permanent*. The following table shows the names, number, and dates of eruption of the temporary and permanent teeth.

Table of Dates in Months of Eruption of Milk Teeth.

Molars.	Canines.	Incisors.	Canines.	Molars.
24 12	18	9 7 7 9	18	12 24

Table of Dates in Years of Eruption of Permanent Teeth.

Molars.	Bicuspid.	Canines.	Incisors.	Canines.	Bicuspid.	Molars.
17 12 to to 6 25 13	10 9	11 to 12	8 7 7 8	11 to 12	9 10	12 17 6 to to 13 25

A tooth is developed partly from the epiblast lining the mouth of the embryo and partly from the mesoblast beneath it; the enamel being of epithelial origin, and the dentine, crusta petrosa

and pulp, of mesoblastic. The *first stage* in the development of the milk teeth is marked by a thickening of the epithelium of the gum in the line of eruption of the teeth, forming the *dental ridge*, and this is accompanied by a growth of the deeper part of the epithelium into the connective tissue below. This down-growth

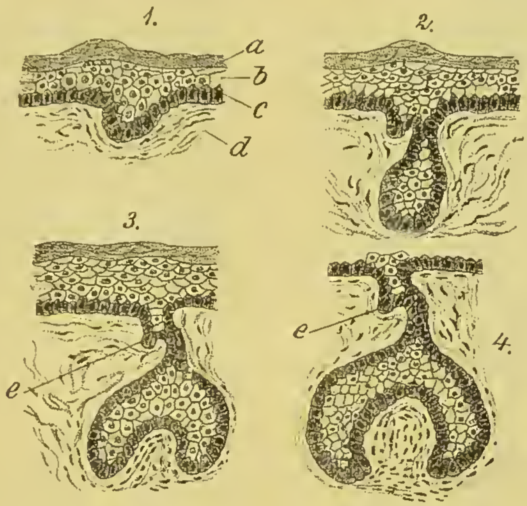


Fig. 72.—Sections of Jaw of Fœtal Mouse, showing early stages of Developing Milk Tooth.

a, Stratum corneum and *b*, stratum Malpighii of gum; *c*, germinal layer of stratum Malpighii; *d*, sub-epithelial connective tissue; *e*, germ of permanent tooth. 1, Stage of common enamel germ; 2, stage of special enamel germ; 3, stage of enamel organ; 4, more advanced stage of enamel organ.

of epithelium is divisible into two—the *labio-dental strand* and the *common enamel germ* or *dental lamina.* The temporary teeth are developed in connection with flask-shaped down-growths of the latter, occurring at intervals, and the permanent in connection with similar down-growths from the necks of the temporary or from the dental lamina in close proximity. The three permanent molars, however, are developed independently from a backward prolongation of the dental lamina. The *second stage*, or that of the *special enamel germ*, is characterised, as just stated, by a series of flask-shaped down-growths (in the position of the future teeth) from the common enamel germ. These down-growths consist of cells of the stratum Malpighii, of which the outermost layer is formed of cubical germinal cells, and those within these are polygonal. From the neck of each flask a small projection may

be seen indicating the point of origin of the permanent tooth. The connective tissue surrounding the enamel germ tends to assume a somewhat laminated disposition, and subsequently constitutes the *dental sac.* The *third stage* is characterised by the growth of a connective tissue papilla from below invaginating the flask; except for this the enamel germ is not changed. The *fourth stage* is characterised by the growth of the papilla and the development of the enamel germ to form the *enamel organ.* The germ is increased in size and becomes more invaginated, and at the same time its central cells undergo degeneration and become mucoid in type, *i.e.*, branching cells with delicate processes. The cells immediately next to the outer layer of cubical cells remain undifferentiated. A section through the invaginated enamel organ thus shows five layers of cells:—(1) Cubical, (2) undifferentiated, (3) degenerated, (4) undifferentiated, (5) cubical. The papilla consists of round embryonic cells for the most part, with but little fibrillar element. It contains capillary blood-vessels, and the cells at its outer aspect have already assumed somewhat the characters of odontoblasts. The *fifth stage* is characterised by the commencement of the formation of the enamel and dentine; the cells of the enamel organ in contact with the papilla, or pulp, as it may now be called, undergo lengthening till they form a row of elongated cells placed palisadewise upon it. These cells have their nuclei in their outer part, and are termed *enamel cells.* The rest of the layers of the enamel organ outside this gradually atrophy but remain for a time as a membranous cap (Nasmyth's membrane), which disappears when the tooth pierces the gum. The enamel cells now commence

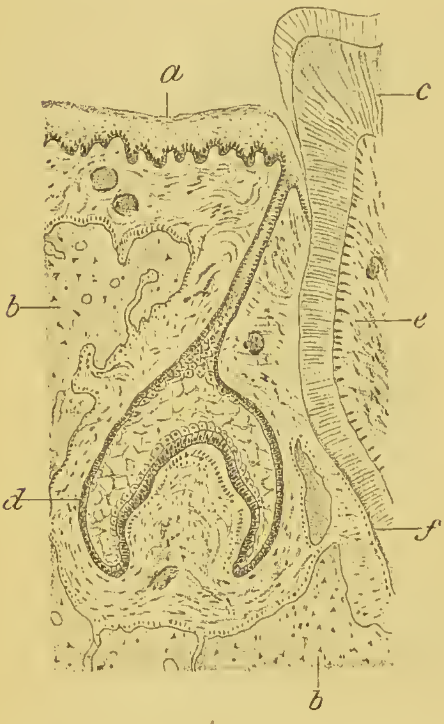


Fig. 73.—Section of Jaw of Kitten, showing Milk and Developing Permanent Tooth.

a, Epithelium of gum; *b*, bone of alveolus of jaw; *c*, milk tooth; *d*, permanent tooth, enamel organ stage; *e*, odontoblasts lining pulp cavity of milk tooth; *f*, crusta petrosa of milk tooth.

to form the enamel, and the odontoblasts the dentine, the two layers of cells thus being carried further and further apart. The

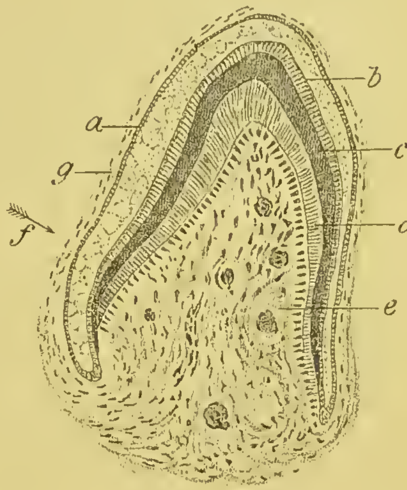


Fig. 74.—Transverse Section of Developing Tooth of Kitten, showing Formation of Enamel and Dentine.

a, Outer layer of enamel organ; *b*, inner layer of enamel organ (enamel cells); *c*, enamel; *d*, dentine; *e*, pulp of tooth, with odontoblasts at periphery; *f*, part from which Fig. 75 is taken; *g*, fibrous sac.

method of the formation of the enamel prisms is somewhat peculiar. The inner end of the cell becomes calcified, but not

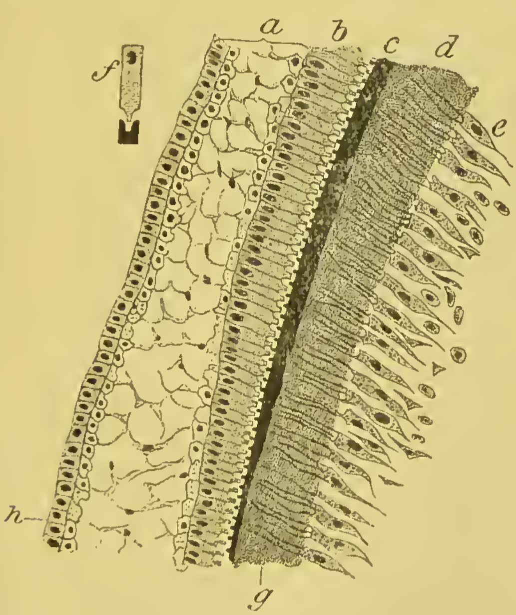


Fig. 75.—Section of Developing Tooth of Kitten.

a, Atrophying layers of enamel organ; *b*, enamel cells; *c*, enamel; *d*, dentine; *e*, odontoblasts; *f*, enamel cell, under a higher power, showing calcified portion (enamel) detached from uncalcified; *g*, points to position of incremental line running parallel with the surface of the dentine (the line has been omitted inadvertently); *h*, cubical outer cells of enamel organ, continuous with enamel cells (*b*) below.

right through, and the uncalcified core of the inner end may be drawn from the calcified portion as from a sheath. As the cell

calcifies at its inner end it undergoes compensatory growth in length, and thus the enamel prism results.

The development of the permanent teeth is precisely similar to that of the temporary. Flask-shaped down-growths from the neck of the temporary tooth develop into enamel organs, and these into young teeth, as already described. As the young secondary permanent tooth develops, it gradually grows into the socket of the milk tooth which it is to displace, causing absorption of it from below and steadily pushing it outwards.

CHAPTER III.

THE PHYSIOLOGY OF MUSCLE.

MUSCULAR tissue is composed of muscle cells, supported by connective tissue containing blood-vessels, lymphatics, and nerves. It is striated or non-striated voluntary, *i.e.*, under the influence of the will or independent of it. Striated muscle is voluntary, except where it forms the heart wall, while non-striated is involuntary, except in the bladder and ciliary muscle.

Non-striped muscle occurs, generally speaking, where movement is slow and involuntary, *i.e.*, not under the control of the will. Thus it is found forming the muscular wall of the stomach and intestines; in the walls of arteries, veins, and lymphatics; in many tubes, such as the ureter, the vas deferens, the Fallopian

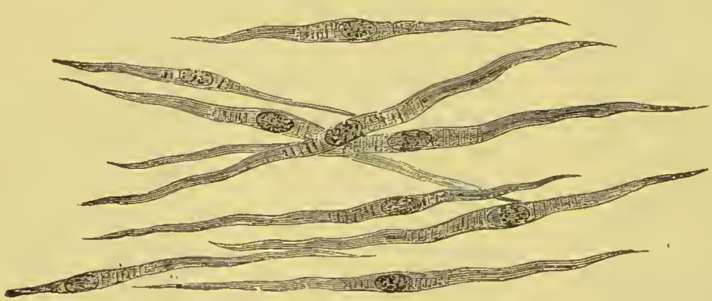


Fig. 76.—Non-Striped Muscle Fibres, Isolated.

tubes, and uterus; in the capsule of the spleen, and lymphatic glands. As already stated, when it forms the wall of the bladder and the ciliary muscle of the eye, it is under the control of the will. The cells are slender and tapering, being $\frac{1}{600}$ to $\frac{1}{120}$ inch in length and $\frac{1}{6000}$ to $\frac{1}{2500}$ inch in diameter. But they vary much in different animals and different situations. They have a distinct cell envelope, which, however, is not separable from its contents. Transverse creases occur in the envelope, which have no relation to the protoplasm of the cell, which exhibits faint

longitudinal striation. The nucleus is oval or elongated, and a few granules are to be seen at its poles, which lie in the long axis of the cell. The cells lie parallel with each other, overlapping instead of being joined end to end, and are united together by cement substance. The muscle is invested by fibrous tissue, from which proceed septa into its substance, dividing it into fasciculi. The blood supply is not so free as in the case of voluntary striped muscle.

Fig. 78. — Transverse Section of Non-Striped Muscle Fibres of Intestine of Dog ($\times 320$).

c, Muscle fibre; *n*, nucleus.

Striped Muscle constitutes the skeletal muscles, which are voluntary, and also the muscle of the heart, which is not under the control of the will. The histological characters of the muscle is different in the two cases.

Fig. 77.–Striped Muscle Fibre of Frog ($\times 140$).

p, Conical end of sarcous substance retracted within the sarcolemma, *s*; *s′*, sarcolemma covering the end of the fibre where it joins the tendon, *t*; *m*, plication of sarcolemma; *c*, individual fibrils.

Ordinary striped or **skeletal muscle** consists of bundles of fasciculi invested by connective tissue sending septa between them, the septa in turn breaking up to pass between the individual fibres. A muscle cell is elongated, being 1 to $1\frac{1}{2}$ inch in length, and about $\frac{1}{2400}$ to $\frac{1}{480}$ in breadth. It terminates at either end in a blunt-pointed extremity, which is attached to the supporting connective tissue. The cells overlap, as in the case of non-striped muscle, and are not joined end to end. The cell wall forms a definite envelope, the *sarcolemma*, adherent during life but readily separable after death. It is very thin, elastic, homogeneous, and translucent. Between it and the cell substance proper are to be found numerous oval nuclei, frequently surrounded by a little undifferentiated protoplasm, their long axis lying in that of the cell itself. But it must be noted that in other animals their disposition may be different. Thus in the

amphibian they are scattered throughout the cell, while in the muscle fibres of some insects they are found in linear series in its axis. The fibres are grouped together into fasciculi, and these again into larger bundles. The sheath of connective tissue surrounding the whole muscle is termed the *epimysium*, that passing from it between the bundles the *perimysium*, while that penetrating between the cells themselves is termed the *endomysium*. At the distal end of the muscle, the connective tissue becomes continuous with that investing the tendon, or with the tendon fibres themselves. The tendon fibres also become united directly with the conical ends of the muscle fibres, but only through the sarcolemma, not with the cell contents. Between the muscle cells an extensive capillary network exists, together with lymphatics and nerves. The capillaries run longitudinally and anastomose by transverse branches, the larger vessels, nerves, and lymphatics being found in the perimysium and epimysium. The lymphatics start in the cell spaces in the connective tissue between the muscle cells, so that the tissue is freely percolated by lymph—external, however, to the sarcolemma. Beneath each sarcolemma is found an oval *muscle-plate*

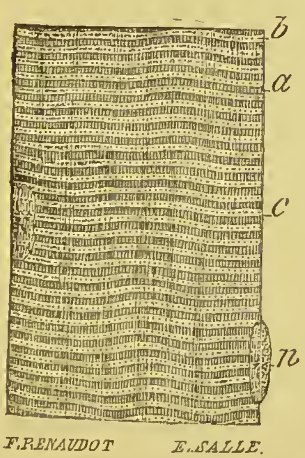


Fig. 79. — Muscle Fibre from Great Adductor of Rabbit.

a, Dark stripe; *b*, Dobie's line; *c*, clear portion on either side of Dobie's line; *n*, nucleus in profile.

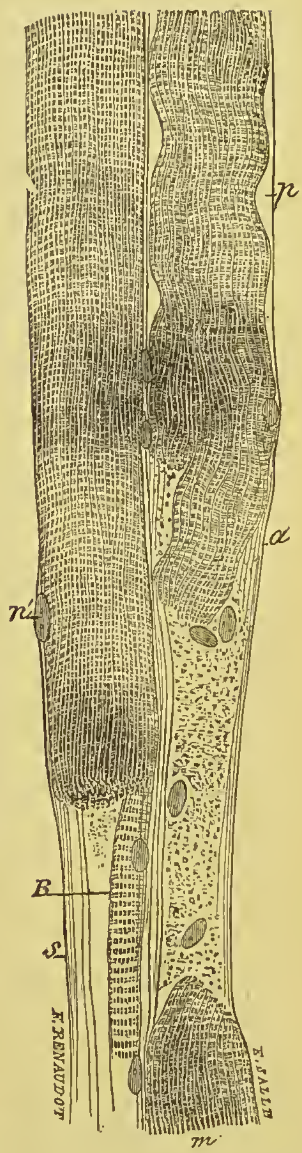


Fig. 80. — Two Muscle Fibres (Ruptured) from Great Adductor of Dog.

m, Sarcous substance; *n′*, nucleus seen in profile; *s*, *a*, sarcolemma; *p*, space between the sarcolemma and the sarcous substance, occupied by fluid; *B*, narrow strand of sarcous substance still adherent to sarcolemma.

—the nerve termination. The protoplasm of the fibres exhibits both a well marked transverse striation, from which this type of muscle receives its name, and faint longitudinal markings, which gives the fibre a distinctly fibrillated appearance. The transverse bands are separated by clear discs, which show a central narrow dark band commonly called Krause's membrane. This cannot, however, be a genuine membrane, as Kuhne observed a small worm, the *myorectes*, travelling up the interior of the fibre, a progress which could not have taken place if any obstructions, such as membranes, had been present. It is more probable that the line is due to the lateral apposition of a series of granules lying in the clear substance — Dobie's granules and line (Fig. 79).

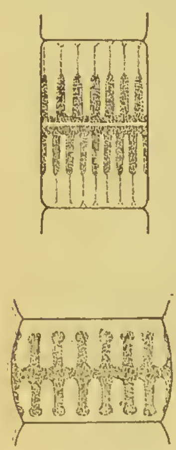


Fig. 81. — Diagrams of a Sarcomere in an Extended and Contracted Condition.

In transverse section a muscle fibre exhibits a series of polygonal areas—Cohnheim's fields—separated more or less distinctly from one another by lines of a supporting or interstitial substance — the sarcoplasm. The intersections can be rendered more distinct by staining the specimen with chloride of gold. The irregular dark areas or Cohnheim's fields apparently correspond to the transverse section of longitudinal muscular columns or sarcostyles. By the use of certain reagents, such as dilute acids, the columns can be broken up into transverse discs, or sarcomeres, the separation taking place at the line of Krause's membranes, and though this cleavage is probably artificial it gives us a conception of what is probably the essential unit of the fibre. Each sarcomere contains a dark transverse band — the sarcous element — which, according to Professor Schäfer, possesses longitudinal diverticula which pass into the clear area lying between the sarcous substance and Krause's membrane. While in the extended condition of the fibre the clear band appears comparatively broad, it becomes greatly reduced in size during the phase of contraction, probably from the absorption of the contents into the sarcous substance.

The sarcous element in each sarcomere appears also to be really double, for in the fully extended condition of the fibre a distinct line can be made out in the middle of the dark band called Hensen's line.

The writer had the valued privilege some years ago of person-

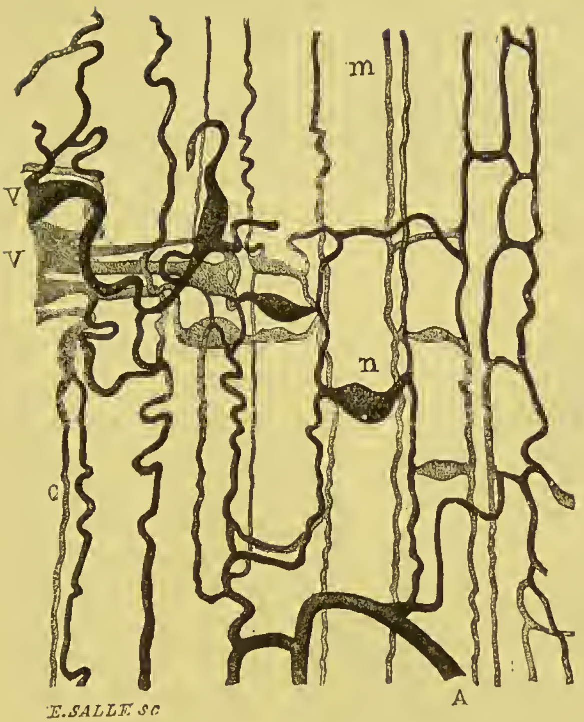


Fig. 82.—Vascular Network of Rabbit's Skeletal Muscle, Injected.

A, Artery; *V*, veins; *n*, dilatation on a transverse capillary branch; *c*, capillary; *m*, meshes of network in which the muscle fibres lie.

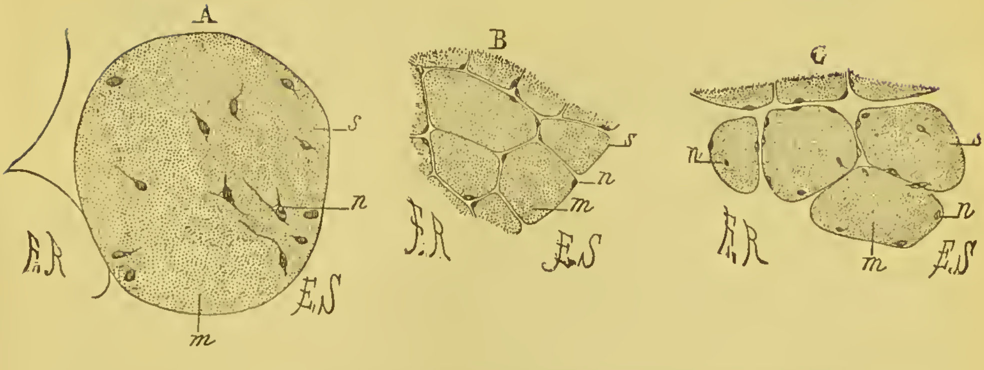


Fig. 83.—Transverse Section of Striped Muscle Fibres.

A, Of frog; *B*, of rabbit; *C*, of another muscle of the same animal (×100); *m*, muscular substance; *n*, nucleus; *s*, sarcolemma.

ally working with Professor Rutherford when he was engaged upon his research, and of verifying his results in a series of specimens of extreme beauty.

1. The extended fibril.—In an untcased fibre, the stripes from which it derives its name are transverse; that is, they run at right angles to the long axis of the cell, and are caused by the lateral apposition of the segments, light and dim, of the individual fibrils. One of these examined alone reveals that it is composed of alternating light and dim segments, the length of which, however, runs in the long axis of the fibril. Thus, in a palisade, though the whole runs horizontally, the stakes of which it is composed are vertical to the ground. The length of the segments relatively and absolutely varies much, however, with the degree of extension or contraction of the fibril. In the extended fibril (Fig. 87, A) the dim segment stains deeply with the reagent, while the light is only affected in part. The length of the *dim segment, Bowman's element* (*b*), is a little less than that of the light. It is cylindrical in shape, with an expansion at either end and a node in the middle of the shaft. The dimness is due to the presence of *chromatin*, a substance staining deeply with reagents, which moves to the ends of the segment during contraction, leaving the body of the shaft clear. There is no doubt a delicate membrane surrounding the segment and defining its shape. It is too thin to be visible, but its existence may be inferred by the action of acetic acid (see below). The *light segment* in the extended fibre may be sub-divided into the *intermediate segment* (*i*) and the *clear segment proper* (*c*) on each side of it. The former is shorter than the dim segment, and at its equator is found *Dobie's*

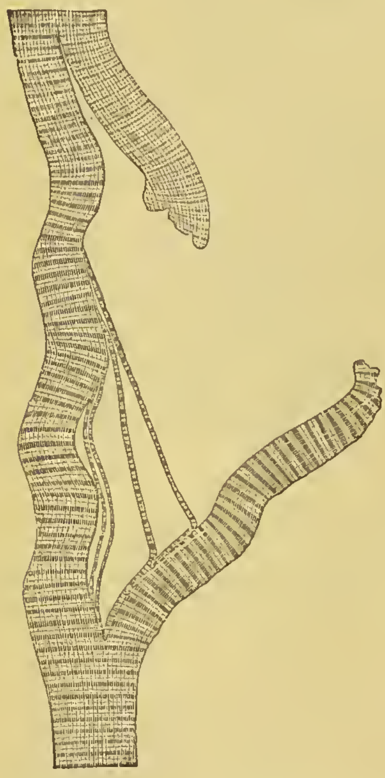


Fig. 84.—Part of a Striped Muscular Fibre of a Calf, teased in white of Egg, and showing Isolated Bundles of Fibrils (×200).

globule (*d*), which is tripartite, and consists of a transverse septum with a hemisphere on either side of it. Both are composed of chromatin, but the septum stains even more deeply than the adjacent hemispheres. The septum is termed the *intermediate node.* On either side of Dobie's globule is to be found *Flögel's granule* (*f*), a small pear-shaped body composed of chromatin, with the thicker end turned usually towards the globule. Between the ends of Flögel's granule and the heads of Bowman's elements is found the *clear segment proper*, which is distinguished by the absence of chromatin from the fluid protoplasm contained in it. On the addition of acetic acid to the preparation, Bowman's elements swell and become barrel-shaped, there being no constriction in the centre to indicate the existence of a membrane in the region of the node. The intermediate segment shows no swelling, but the clear segment proper is drawn out conformably with the increased area of the end of Bowman's segment. The swelling up of the dim segment is not probably due to the action of the acid on the chromatin, as in the contracted fibre in which the chromatin has passed into the heads of Bowman's element the shaft swells up as before. It is probably due to an action comparable to that of acid upon fibrin, by which acid albumin is produced. Though it cannot readily be demonstrated, it seems probable that both

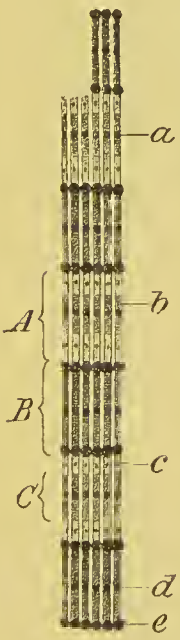


Fig. 85. — STRIPED MUSCLE OF CRAB (EXTENDED) (×450).

A, Light stripe; *B*, dark stripe; *C*, intermediate segment in light stripe; *a*, Dobie's globules; *b*, Nebenseheibe of Merkel; *c*, Flögel's granules; *d*, Hensen's line; *e*, heads of sarcous elements.

Fig. 86.—STRIPED MUSCLE OF CRAB (RELAXED) TEASED (×250).

a, Muscle fibre or portion of one; *b*, fibrils.

the light and dim segments are invested with an exceedingly thin and tough envelope, perhaps merely a modification of the outer part of their substance.

Hensen's line seems to be due not to the presence of a membrane in the equator of Bowman's elements, but to the node found there

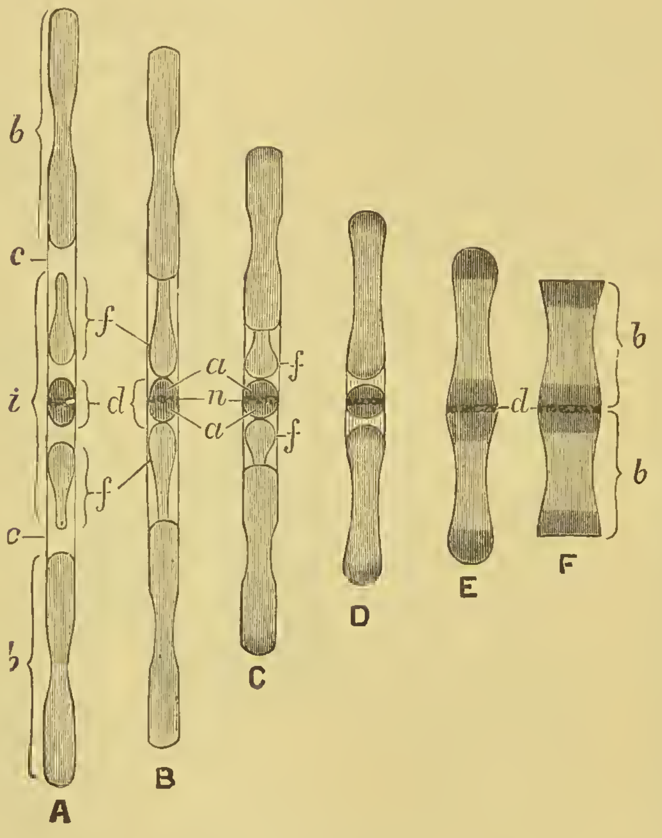


Fig. 87.—Diagrammatic Representation of Changes in a Contracting Fibril of Muscle of Crab.

A, Fibrillar segments extended; *F*, fibrillar segments contracted; *B*, *C*, *D*, *E*, intermediate stages; *b*, dim segment; *i*, intermediate segment; *c*, clear segment proper; *n*, septum of Dobie's globule (*d*); *a*, "hemisphere" on either side of septum; *f*, Flögel's granule.

and to the sarcoplasm between adjacent nodes. The sarcoplasm gives rise to a row of small ellipses, very clearly seen in the contracted fibre (Fig. 88). The fibrils adhere very firmly to each other at the intermediate nodal line, at which point also the sarcolemma is attached.

2. THE UNEXTENDED FIBRIL.—Here the clear segment proper has disappeared, so that the light stripe, in this case represented by the intermediate segments in lateral apposition, is narrower than the dim (Fig. 87, B).

3. THE CONTRACTED FIBRIL.—Contraction takes place between the node at the equator of Bowman's element and the intermediate nodal line. It may be divided into two phases, in the first of which shortening occurs in the intermediate and clear segments, and in the second in Bowman's elements—this being accompanied with reversal of the stripes.

When the clear segment has disappeared, the ends of Bowman's elements come close up to the intermediate segment. Shortening of the intermediate segment itself then takes place, whereby Flögel's granule is lost to view, and the heads of Bowman's elements approach Dobie's globule (Fig. 87, D). The fluid in the shortened segments apparently escapes into Bowman's elements, as no lateral bulging takes place. At the same time it may be noted that a very slight increase of the diameter of the segment is sufficient to account for the fluid at this stage, and as the contraction proceeds the fibrils undoubtedly increase in diameter throughout, as may be clearly seen in the fully contracted fibre. At this stage, before the second phase commences, and before the chromatin has begun to flow towards the heads of the dim segments and a reversal of the stripes to take place, an almost homogeneous appearance is presented by the fibril—the so-called "homogeneous stage" of contraction. When the second

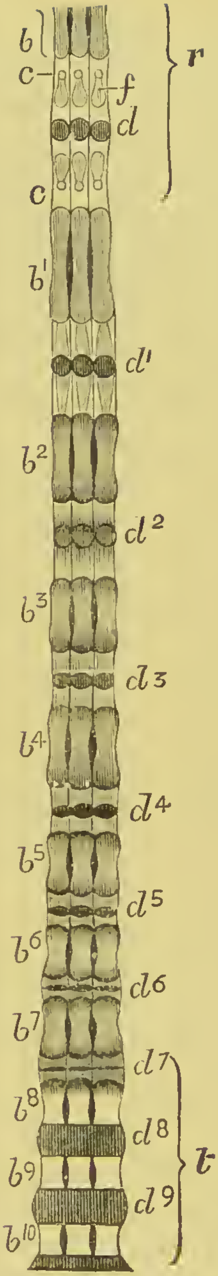


Fig. 88.—THREE FIBRILS OF CRAB'S MUSCLE, SHOWING THE SUCCESSIVE CHANGES FROM PHYSIOLOGICAL EXTENSION (r) TO COMPLETE CONTRACTION (t).

b, b^1–b^7, Dim segments; d, d^1–d^7, Dobie's globules; b^8, b^9, b^{10}, light stripe of contracted fibre, consisting of body of dim segment of relaxed or extended fibre; d^8, d^9, dark stripe of contracted fibre, consisting of the heads of Bowman's elements and Dobie's globules, with other elements of the intermediate segments; f, Flögel's granules; c, clear segment proper.

phase commences the chromatin flows to the ends of Bowman's elements, which it causes to swell up, leaving the shafts clear. Ultimately the swollen ends of the dim segments and Dobie's globule become sufficiently fused for the intermediate nodal line to be no longer distinguishable. Complete reversal of the stripes has now taken place, the dim stripe of the contracted fibre corresponding to the heads of Bowman's elements and Dobie's globules, with other elements of the intermediate segments, while the light stripe is represented by the clear shafts of Bowman's elements, which have lost their chromatin (Figs. 87 and 88).

The effect of acetic acid upon the contracted fibril tends to confirm the theory of the reversal of the stripes, inasmuch as the light stripe now swells, showing that it is not the light stripe of the uncontracted fibril. The now dim stripe is unaffected.

It may be that Bowman's elements are the really active parts concerned in contraction, causing absorption into them of fluid from the clear and intermediate segments, whereby these are shortened, and shortening themselves by a forcible rearrangement of their micellæ, by which the chromatin is pressed to the ends, while the absorbed fluid is retained in the micellar network.

Effect of curvature on the microscopical appearances of muscle.—The apparent reversal of the stripes which takes place in the semi-contracted or contracted fibre, in focussing up and down, is comparable to the effect produced in similar circumstances in the case of a red blood-corpuscle, and must not be confused with the real reversal already referred to. At one focus the ends of Bowman's elements and Dobie's globules appear light, and the shafts of Bowman's elements dark, and at another the appearance is reversed.

The old theory that the stripes were merely due to differences of curvature in the fibril—that the latter was merely to be regarded as a homogeneous varicose filament—has of late years been revived by Haycraft, who bases his views upon the results of impressions upon collodion which exhibit appearances corresponding to Dobie's and Bowman's stripes. The writer has criticised this view elsewhere, and would only now remark that such a theory entirely passes over the effect of staining reagents upon the chromatin and the action of acids upon the intermediate and Bowman's segments.

Development of muscle cells.—Muscular tissue is developed in the mesoblast on either side of the neural canal. The cells elongate, become multinucleated, and exhibit a distinct envelope.

The protoplasm then becomes longitudinally fibrillated, the fibrillation commencing at one side of the fibre usually and spreading round it.

Termination of motor nerves in muscle.—The *end-organs*, or end-plates, already referred to, are oval flattened masses of protoplasm, and lie immediately upon the fibrils beneath the sarcolemma. The granular protoplasm containing many clear nuclei is termed the *bed* or *sole* of the organ, and receives the termination of a medullated nerve fibre. The *grey sheath* of the latter becomes continuous with the sarcolemma, and the *medullary sheath* and *axis-cylinder* divide beneath it to two or more primary branches.

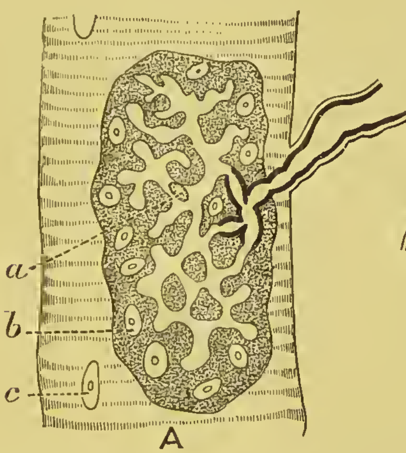


Fig. 89, A.—End-Organ of Nerve in Voluntary Muscle Fibre of Lizard highly magnified.

a, Nucleus of "arborescence"; *b*, nucleus of "sole"; *c*, nucleus of muscle cell.

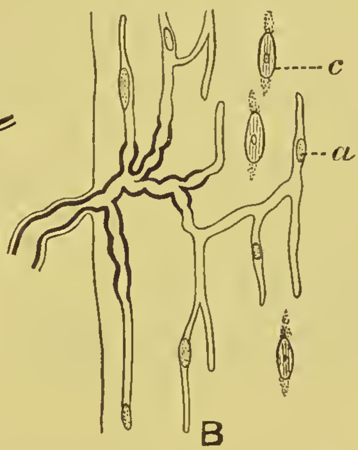


Fig. 90, B.—End-Organ of Nerve in Voluntary Muscle Fibre of Frog.

a, Nucleus of arborescence; *c*, nucleus of muscle cell (after Kühne).

The medullary sheath now suddenly ceases, the axis-cylinder continuing to branch in a more or less arborescent way: the trunks of the tree anastomosing with each other, and the terminal branches ending in a club-shaped fashion. Granular nuclei are found here and there on the branches of the axis-cylinder.

In **cardiac muscle** the cells are cylindrical in shape and branched towards one end. The ends are serrated, and join directly with those of adjacent cells to form a network. They are much smaller than the cells of skeletal muscle, especially in length, and have no separable sarcolemma. Each muscle cell possesses one oval nucleus, which is placed in its centre, granules

of pigment being often found at the poles, especially in old age. Delicate connective tissue is to be found between the cells, con-

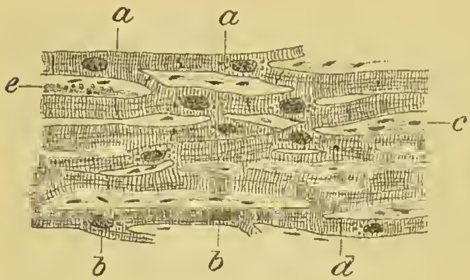


Fig. 91.—Longitudinal Section of Cardiac Muscle (Human) (× 200).

a, Muscle cells; b, nuclei of same, with yellow pigment at poles; c, fibrous tissue between muscle fibres; d, junctions of segments of muscle; e, capillary blood-vessel.

Fig. 92.—Vertical Section of Heart Wall (Human) (× 200).

a, Transverse section of cardiac muscle fibre; b, connective tissue supporting them; c, endocardium.

tinuous with that of the endocardium and pericardium, and supporting blood-vessels, lymphatics, and nerves. Differentiation

Fig. 93.—Transverse Section of Cardiac Muscle Fibres of Ventricle of Calf (× 550).

Fig. 94.—Fragment of the Network of Purkinje from the Ventricular Endocardium of the Sheep (× 300).

c, Cell; f, striated substance; n, nucleus.

of the protoplasm of the cell into longitudinal fibrillæ has commenced at the periphery, but has not extended through the cell

substance, so that though they exhibit longitudinal and also transverse striation, they cannot be split up into fibrillæ. *Purkinje's cells* are found beneath the endocardium of the ventricles. They are large quadrangular cells, with one or two nuclei, the outer part of the protoplasm being striated.

Amœboid movement and contraction of muscle.—It would appear that muscular movement is an instance of contractility displayed only in one axis, as opposed to the less specialised contractility of the amœba, which may take place in any direction; the term "contractility" being used in its widest sense to indicate a translocation of particles, whereby there is a change in their relative position, but no change in the bulk of the tissue of which they form a part. The muscle cell in common parlance is said to contract when it shortens, but if we employ the term contraction in its widest sense, the return of the fibre to its normal length—the "relaxation" of the fibre—is as much an essential part of the contraction as the shortening itself. This relaxation, by which the fibre recovers its previous shape after shortening is over, is sometimes attributed to its elasticity, but there seems no reason for regarding the extended condition of the fibre as more "normal" to it than its contracted, or to suppose that mere elasticity would enable it to pass more readily from the contracted to the extended state than from the extended to the contracted. Were contractility evidenced in only the one direction of shortening, it would appear that the inevitable result of repeated continuous contraction would be to cause the muscle to become flattened in its equatorial plane, and so of no further use. The amœboid cell may become flattened by contractility, but it recovers its original form or assumes some new one by the exercise of the same power. In the amœboid cell, as already pointed out, the condition of activity, *i.e.*, contractility, is evidenced both by the pushing out of pseudopodia and their withdrawal, while the condition of rest is associated with the spherical state. At the same time, in virtue of the contractility being not limited to activity in one axis, but being possible in any, if the cell is strongly stimulated—so strongly that all its parts are affected—its shape still remains spherical; its particles being all equally stimulated have no tendency to assume different relative positions. And as contraction, for all practical purposes, does not imply any change in bulk, the cell during strong stimulation, as opposed to the muscle cell, assumes the same form as when it is at rest.

Examination of muscle fibres by polarised light.— When examined with crossed Nicol prisms, parts of the fibril are seen

to be *anisotropic* (doubly refractile) and parts *isotropic* (singly refractile). In the uncontracted fibril, Bowman's elements, Dobie's globule, and Flögel's granule (if present) are anisotropic, while the clear segment proper and the interstitial sarcoplasm are isotropic. In the contracted fibril the shaft of Bowman's element is still bright, *i.e.*, anisotropic, though less so than before, and the now dim stripe is highly anisotropic, *i.e.*, composed of a highly doubly-refractile substance, the *tissue* of Bowman's elements being itself doubly refractile, but less distinctly so. The clear segment proper is always singly refractile, while the shaft of the intermediate segment varies, according to whether it contains Flögel's granule or not; in the former case being anisotropic and in the latter isotropic.

The **elasticity of muscle.**—The elasticity of a substance—that is, the degree of readiness with which it undergoes changes in form

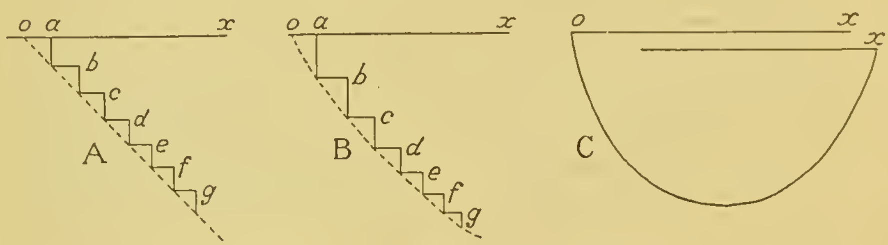


Fig. 95.

A, Curve of elasticity from an inorganic body (india-rubber); *B*, curve of elasticity from sartorius of frog; *C*, curve of elasticity produced by continued extension and recoil of frog's muscle; *o x*, abscissa.

and recovers its previous form when the exciting cause is removed—varies in different cases. It is defined in terms of its *amount* and *quality*. Thus when a substance is readily altered in form its elasticity is said to be small in amount. The elasticity of an india-rubber band is small in amount, as it is readily stretched, whereas that of a billiard ball is great, as it does not readily undergo change of shape. The quality of the elasticity in the two cases is as different. Inasmuch as the india-rubber band readily regains its original form when released from the influence of the extending force, or an india-rubber ball when a compressing force is removed, the elasticity of india-rubber is said to be perfect in quality; but the elasticity of a billiard ball, though great in amount, is very imperfect: if its shape be once altered the original form is not recovered. The elasticity of muscle is small in amount but perfect in quality. It is readily extended, and the original

form is readily recovered, provided the stretching force has not been too great. It thus resembles the india-rubber band, but it is to be noted nevertheless that there is a difference between the curve of extension and recoil of muscle and that of the india-rubber band. Whereas the addition of equal increments of weight produce in the latter an equal extension, in the case of muscle the extension is not proportional to the extending force, but with equal increments of weight becomes progressively less till a limit is reached, after which the muscle ruptures. In other words the extension in the case of inorganic substances is directly proportional to the extending force; in organic it is not so, but becomes progressively less. If a record be taken by means of a style moving upon a smoked surface adjusted by hand, it is found that in the case of the india-rubber band a straight line is obtained by the junction of the apices of the angles, but in the case of stretched muscle the line is a hyperbolic curve (Fig. 95). If the weight used be too heavy—that is, if the *limit of elasticity* be passed—the muscle will not recover its original length at once. This is shown in the figure, in which, after the weights were progressively removed, the writing point does not regain the abscissal line. This is called the *elastic after-effect*, and must not be confused with the *rupture point* of muscle. A frog's gastrocnemius will bear a weight of 1500 grams without rupturing, but a weight of 100 grams is sufficient to prevent it recovering its original length.

The elasticity of a contracted muscle is still less than that of an uncontracted one; that is, an equal weight elongates it to a greater degree.

The **uses of the elasticity of muscle.**—Normally the muscles are in a state of slight tension through their elasticity, and this avoids delay in their action upon their point of insertion. Were it not for this time would elapse while a certain amount of "slack" was taken up, and response would not be immediate. Elasticity also prevents the occurrence of shock, which would inevitably result were the force applied through an inextensible rigid medium.

The **excitability of muscle.**—Muscle is *excitable* or *irritable*, That is to say, it will respond to stimulation; and the stimulating force may act upon the muscle fibres directly or through the medium of the nerves. The response takes the form of *contraction*, as it is called; and the amount of contraction, within certain limits, is proportional to the strength of the stimulus. Stimulation or excitement, whereby the muscle undergoes changes

in shape, termed contraction, may be produced by various agencies. Normally the force is nervous; that is, it is generated in nerve cells and transmitted by nerve fibres to the motor end-plates of the muscle, and thus to the fibrils themselves. But other forms of stimulation will also excite contraction, such as chemical, thermal, and mechanical. The stimulus commonly employed in physiological experiments on the excited muscle is electricity.

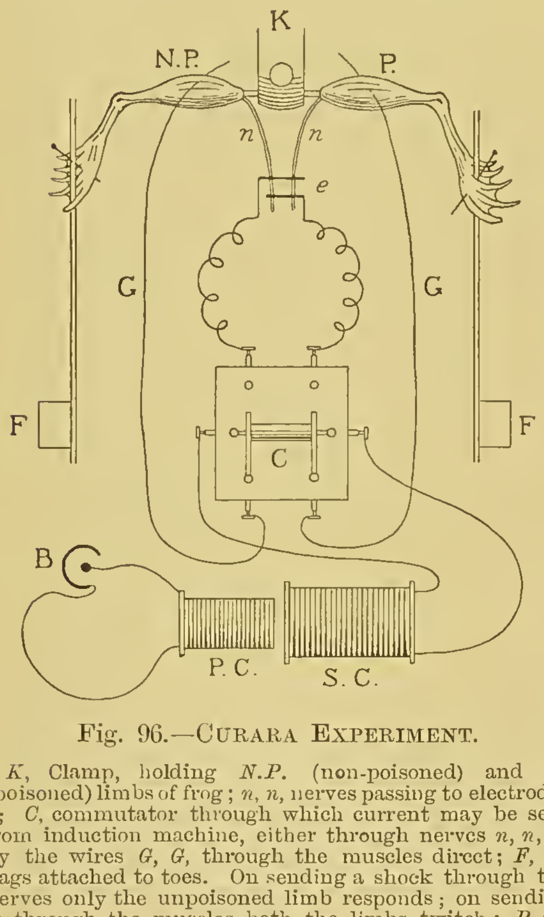


Fig. 96.—Curara Experiment.

K, Clamp, holding *N.P.* (non-poisoned) and *P.* (poisoned) limbs of frog; *n*, *n*, nerves passing to electrodes *e*; *C*, commutator through which current may be sent from induction machine, either through nerves *n*, *n*, or by the wires *G*, *G*, through the muscles direct; *F*, *F*, flags attached to toes. On sending a shock through the nerves only the unpoisoned limb responds; on sending it through the muscles both the limbs twitch; *P.C.*, primary coil; *S.C.*, secondary coil; *B*, battery.

That the stimulus will act either upon the muscle directly or through the medium of the nerve may at first sight be open to question, because the stimulus, though applied not to the nerve trunk but to the surface of the muscle itself, might act through exciting the smaller microscopic nerve filaments running between the individual fibres, or the end-organs beneath the sarcolemma themselves. It thus becomes necessary by experiment to exclude the action of the nerve elements altogether, and this is done by means of *curara*, which paralyses the motor nerve terminations themselves. If the brain of a frog be pithed, and a solution of curara (Indian arrow poison) be injected beneath the skin of the back into the dorsal lymph sac, it is found that in half-an-hour or an hour's time the animal has become flaccid and will make no voluntary movement; nor will pinching of the toes or stimulation of the skin excite reflex action. If the skin of the leg on either side be now removed, and the sciatic nerve laid bare and stimulated, no contraction of muscles of the leg supplied by it takes place,

whereas if the electrodes be applied directly to the gastrocnemius a very marked contraction is the result. But it may still be argued that the poison has acted upon the nerve trunk, and that the nerve terminations are still intact, and that these are the elements stimulated by the direct application of the electrodes to the muscle, so that a further experiment to show that the nerve trunk itself is unaffected becomes necessary. In a second frog, pithed as before, the sciatic nerve is exposed on one side, say the right, a ligature is passed beneath it and tied firmly round all the other structures of the leg, and the animal curarised. In a short time flaccidity will be observed, except in the right leg, through which the poison has not circulated. If the toes of the leg are pinched the foot is drawn up, but no such reflex action is to be found on pinching the toes of the left leg. If the skin be removed from both legs and the left sciatic nerve exposed, then on stimulating the right sciatic, contraction results, whether the stimulus be applied above or below the seat of ligature; but stimulation of the left sciatic gives no result. Direct stimulation of the muscle on either side gives rise to contraction. That the poison has not acted upon the nerve trunk is evidenced by the fact that when the nerve on the right side is stimulated above the seat of ligature, *i.e.*, in a part through which the blood has circulated freely, carrying the poison with it, contraction results. It thus appears that the failure of contraction must be attributable to the poison acting on some part lower down.

Two confirmatory experiments may be performed to show that it is the *motor nerve terminals* which are probably affected. If a muscle be removed from the general circulation by its blood supply being ligatured, and the frog be then curarised as before, subsequent stimulation of the nerve supplying the muscle gives rise to contraction, though its *whole course outside the muscle* has been exposed to the action of the poison. Again, if in another frog the sciatic nerve be divided high up, and dissected out down to the gastrocnemius, and carefully raised before the poison is injected, so that no blood reaches it, stimulation of the cut end, or of any of the extra-vascular length, leads to no contraction. These experiments all lead to the conclusion that the poison acts at some point *between* the nerve trunk and the muscle fibrils themselves, probably upon the motor nerve terminations.

On stimulation of muscle, or the nerve going to it, the resulting contraction varies in character with the nature of the stimulus and the way it is applied. There are two kinds of muscular contraction: (1) the *simple twitch*, which is almost instantaneous, and (2) the *tetanic contraction*, which is much more prolonged, the

shortening continuing for a greater or less length of time, made up in reality of a number of simple twitches following each other in rapid sueeession.

Nerve-muscle preparation.—In applying any stimulus to a musele, direetly or indireetly, it is more eonvenient to separate it first from the body than to use it *in situ.* The muscle of a frog is usually taken, as, being a eold-blooded animal, it retains its irritability for a greater length of time after removal from the body. The musele usually selected for eonvenienee is the gastroenemius; the tendo Achillis is retained to serve as a point of attaehment for the thread going to the lever and the lower end of the femur, by which the musele is fixed in the elamp. The seiatie nerve has been disseeted out as high as possible, and also retained. Sueh a musele preparation may be stimulated either direetly or indirectly by thermal, ehemical, or mechanical stimuli, but mueh more usually electrieity is employed. Eleetric foree is generated in a battery, and the eonstant current produeed by the battery itself may be used as a stimulus, or the induced eurrent from the induetion maehine.

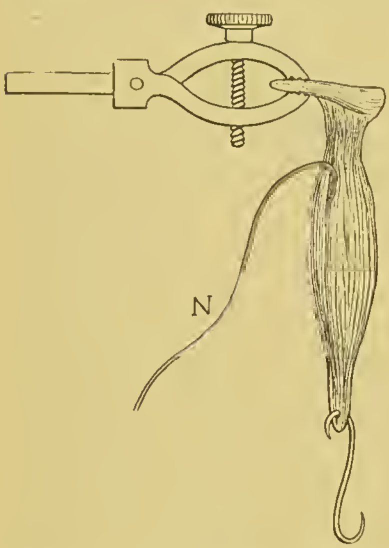


Fig. 97.—Nerve-Muscle Preparation of Frog in Clamp.
N, Nerve.

The Electrical Stimulation of Muscle and Nerve.

The **Galvanic current.**—A battery eonsists of two elements suspended in a fluid. The one of these (sueh as zine) which is easily aeted upon by the fluid is termed the *positive element*, that whieh is not (such as copper) the *negative element.* When these two elements are eonneeted together outside the battery itself by some conducting medium, what is termed a *galvanic action* is set up, and the *current* passes from the positive element in the battery to the negative, then along the conneeting medium outside,

and so back to the positive element. If the conducting medium, which is usually an insulated wire, be divided midway, the current ceases, but on the severed ends being brought together it is re-established. The ends of the cut wire are termed the "poles": that connected with the copper of the battery the *positive pole*, that with the zinc the *negative*. When these poles are used for physiological purposes they are termed *electrodes*.

When the terminals are brought together the *circuit is closed* and the *current made*. When separated, the *circuit is opened* and the *current broken*. The positive electrode is sometimes spoken of as the *anode* (*ανα*, up), while the negative is called the *cathode* (*κατα*, down).

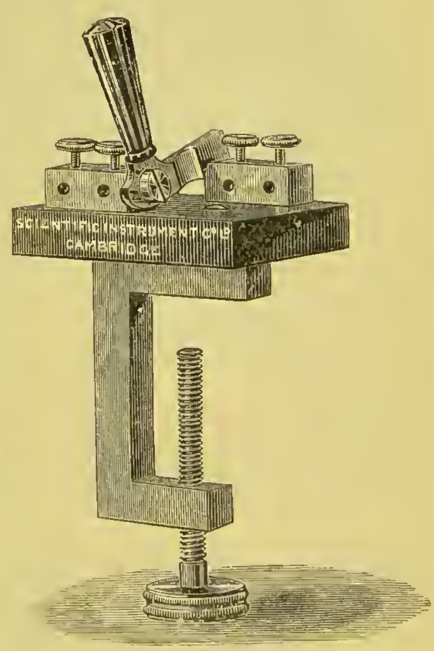


Fig. 98.—Du Bois-Reymond Key.

As in making physiological experiments it is often desirable to remove the tissue from the influence of the current without displacing it from its position or moving the electrodes, certain forms of *keys* are in use, which are placed at some point in the circuit. Keys are used either to *make and break* the current, or to *short circuit* it, and some, such as the *Du Bois-Reymond*, may be used for either purpose. This key consists essentially of two brass plates, with an intervening brass bridge. When the bridge is lowered the two plates are in electrical continuity; when it is raised they cease to be so. The key is placed at the point of interruption in one of the wires, either positive or negative, as shown in Fig. 99. When it is desired to make the current, the brass bridge is tilted into position by means of the handle of the key, and the reverse when it is desired to stop the current. It is thus used (1) as a *make and break* key. But it may also be used for short circuiting. In this case (2) both the wires from the battery may be supposed to be interrupted, the proximal and distal ends of the cut positive wire being fixed to one brass plate of the key by binding screws, and the corresponding ends of the negative wire to the other. When the brass bridge of the key is up there is no connection between the two plates, and the current

passes through the tissue connecting the two electrodes; when the bridge is down the plates are in electrical continuity, and the whole of the current passes through the shorter circuit, thus established, back to the battery, without reaching the terminals of the wires. That is to say, it follows the shorter circuit, and the key is used as a *short-circuiting* key.

The galvanic current, it will be seen, is a *constant* one, *i.e.*, provided the circuit is not broken, it continues till the battery is exhausted. But in physiological experiments the *induced current* is the more commonly employed, and it may be well here to indicate the principles of construction of the *induction machine.*

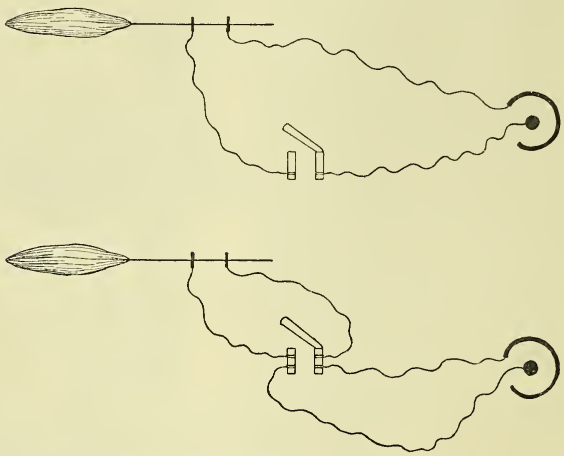


Fig. 99.—Diagram of Du Bois-Reymond Key, used (1) for Make and Break Shocks, (2) for Short Circuiting.

The **induction coil.**—In this instrument the wire joining the two elements of the battery is arranged in the form of a spiral, termed the *primary coil.* Surrounding this slides another spiral, the *secondary coil*, which is, however, quite unconnected with the primary. The terminal wires of the secondary coil are continued as the electrodes. When the circuit of the primary coil is closed and the current thus made, a second or *induced* current is engendered in the secondary coil, but only for an exceedingly brief space of time, and this is termed the *make shock;* similarly when the circuit of the primary coil is opened, another very brief current is induced in the secondary coil, the *break shock.* But no secondary

shock or current occurs while the stream of electricity is flowing through the primary coil. It is only by the making or breaking of the current in the primary coil (or by varying the intensity of the current during the flow) that a secondary shock is induced.

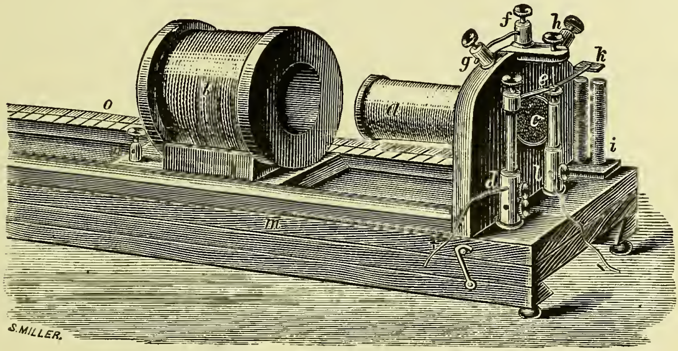


Fig. 100.—INDUCTION MACHINE.

a, Primary coil; *b*, secondary coil; *d*, *l*, binding screws for attachment of wires of primary circuit when the interrupted current is employed; *g*, *h*, binding screws for wires of primary circuit when single induction shocks are required.

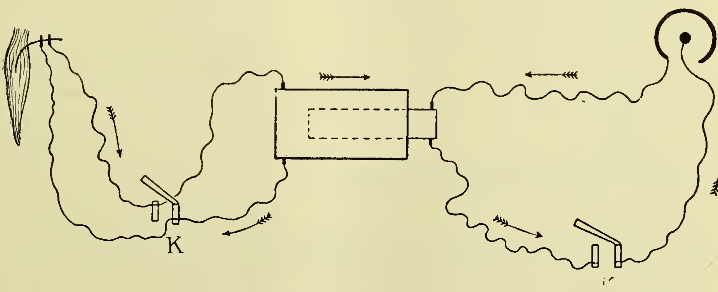


Fig. 101.—SCHEME OF BATTERY, INDUCTION COIL AND NERVE-MUSCLE PREPARATION.

On the left the key *K* is a short-circuiting one placed in the secondary circuit; on the right a make and break key in primary circuit.

The direction of the current in the secondary coil is the reverse of that in the primary on making, but in the same direction on breaking the current.

The current from the battery, on first entering the primary coil and passing along its spirals, gives rise to an induced current in the neighbouring spirals in the opposite direction; and this self-induction in an opposite direction delays the establishment of the full strength of the current, and consequently of the secondary current. No such delay in the *fall* of the current can occur on breaking, as all connection with the battery is suddenly cut off. As a more quickly developed current is more effectual as a stimulus than one developed slowly, the *break shock* is said to be the stronger of the two.

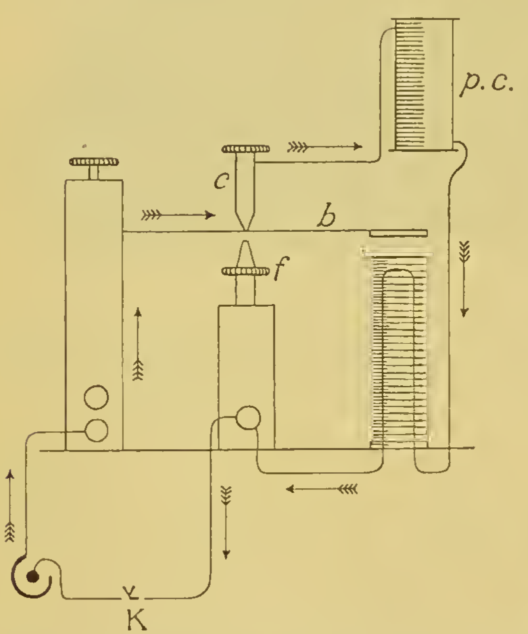


Fig. 102.—Neef's Hammer for Production of the Interrupted Current.

The strength of the induced shock depends on the strength of the battery connected with the primary coil, and also upon the relative position of the coils to each other. Thus the further they are apart the weaker the induced current, which is stronger when the secondary is pushed up so as to completely enclose the primary. It will be noted that there may still be an induced shock even when the coils are some distance apart, but their axes require to be in the same line. No secondary current is induced if the coils are at right angles, and intermediate angles give intermediate strengths of current, the effectiveness of the secondary current being established and increased as the coils are brought into line. In the ordinary induction machine the secondary coil slides upon a groove, so that it is readily pushed over the primary coil, or to some distance from it, or to any intermediate point.

Faradic electricity.—It is sometimes required to apply a rapid succession of make and break shocks, and this is effected by placing an interrupter of the current in the primary circuit (Fig. 102). In this case the current is made and broken by a rapidly-vibrating

steel spring. The vibrations of the spring are maintained by the alternate magnetisation and demagnetisation of two small coils with iron cores placed in the primary circuit. As the current passes through the circuit these become magnetised; they attract the spring, and the current is broken by the disconnection of *c* and *b* (the screw *f* may be neglected in this figure). But this demagnetises the coils; the spring flies back and the current is again made, the alternations being continued indefinitely, and inducing secondary make and break shocks in the secondary coil. This is generally known as the "interrupted current."

Make and break extra currents.—As already stated, the break is stronger than the make induction shock, and the following arrangement (Helmholtz) has been devised for equalising the two. The screw *c* is raised out of reach of the excursion of the spring *b*, and the screw *f* raised till its point comes within the excursion. An extra wire, W, is introduced between *a′* and *c′*. When K is closed the current passes through W and *c′* to the primary coil, and thence by the electro-magnet M and pillar *d* back to the battery. As before, the spring *b* is drawn down by the magnet M, and the current from the battery is short-circuited to a great extent, in that it can now pass from *a′* along *f* and *d*, and so back to the battery; but not entirely short-circuited, for some of it still passes along the wire W, the amount being inversely proportional to the resistance offered, which may be regulated. Thus, though the current in the primary coil is sufficiently reduced to allow the spring to fly back from the magnet, it does not entirely cease, even

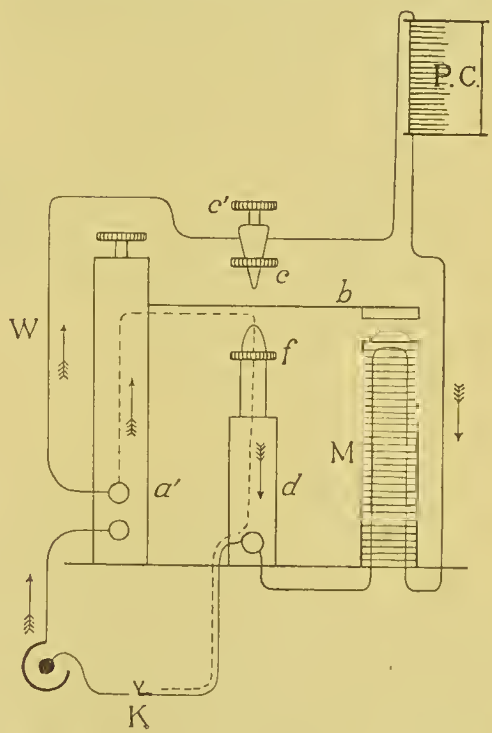


Fig. 103.—Helmholtz's Arrangement for Equalising Make and Break Shocks.

at the break, and hence the induced shock in the secondary coil is not so great; because, as there is still some current left in the primary coil, self-induction takes place at the break as well as at the make, the two shocks being thus brought to the same level. This equalisation of the make and break shocks may as easily be brought about by the introduction of a deriving circuit when only simple make and break induction shocks, without the use of Neef's hammer (steel spring interrupter), are required; and an explanation of the *modus operandi* in this case may perhaps be more easily followed.

Here again there is always some current passing through the primary coil, both when the key K is closed (*cf.* contact *b–f* in Fig. 103) and when it is opened. When the key is closed, part of the current from the battery passes through the coil and part through the deriving circuit; the amount passing through each being inversely proportional to the resistance offered. When the

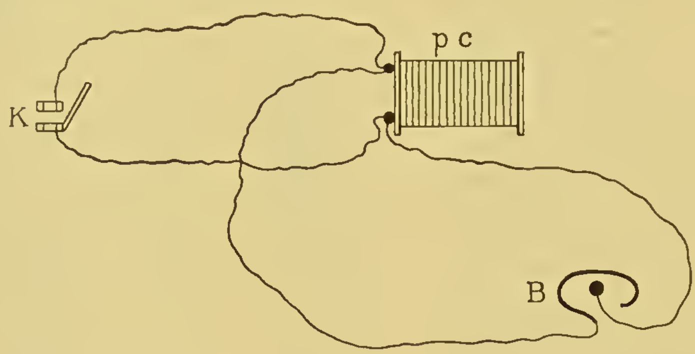


Fig. 104.—Scheme of Arrangement to Equalise Make and Break Shocks.

key is opened all the current passes through the coil, and, as before stated, the self-induced *make extra current* in the *opposite* direction to the main current delays its establishment in full strength. On closing the key there is a fall of current only, not an abolition of it, so that a *break extra current* appears in the primary coil in the *same* direction as the main current and delays the fall in its strength. We have, therefore, in these cases of equalisation of the two shocks, to deal not with a break shock proper, but with a reduced break shock owing to the appearance of the break extra current in the primary coil. As the break shock is thus brought down to the level of the make shock, a stronger current is required to produce the same strength of

stimulus, and this may be attained either by increasing the strength of the battery, or by pushing up the secondary coil.

Stimulation by Galvanic electricity.—If a constant current be sent through a nerve or muscle, contraction of the muscle takes place when the circuit is closed, and again when it is opened; usually none is observable when the current is passing. Stimulation occurs at the negative pole on closure of the circuit and at the positive when it is opened.

In the accompanying Fig., A shows by the arrow and – sign the negative polar, or cathodal region, at which stimulation occurs at closure of the circuit, and B by the arrow and + sign the positive polar, or anodal region, in which stimulation occurs at opening. In either case the wave of muscular contraction starts

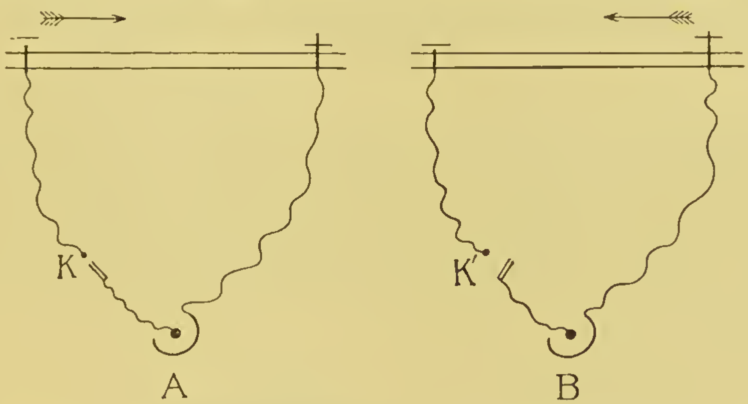


Fig. 105.—Scheme of Stimulation of Muscle by the Constant Current.

at the point of stimulation, and thence sweeps over the length of the muscle. The stimulation at the negative pole on closure is the stronger of the two.

If, however, a sufficiently strong current be sent through a muscle directly, it may be thrown into a continued state of contraction, termed *galvanotonus*, and this results more readily at the make or cathodal shock. And it is to be noted that whereas the rapid induced stimulus of the induced current is more effective in the case of a nerve, the muscle itself, probably from its comparative sluggishness, is more affected by the slower shock of galvanism. On this is founded the "reaction of degeneration" in clinical medicine. When the nerves and their terminals are completely degenerated, the muscle responds more readily to Galvanic as opposed to Faradic shocks.

The peripheral ends of sensory nerves, too, unlike the trunks, are stimulated during the whole passage of the current, if it be strong enough.

That the stimulation of the muscle is due to independent muscular excitability, apart from the nerve endings, is readily proved by eliminating these with curara.

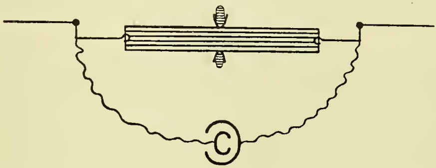


Fig. 106.—Sartorius Clamped in Middle and Attached to Levers at Either End.

The following experiment demonstrates the fact that stimulation starts at the anode on opening, and at the cathode on closing, and that the cathodal stimulation is the stronger of the two.

The sartorius muscle of a curarised frog is dissected out and clamped midway between its ends, sufficiently tightly to prevent any shifting of its position, but not to stop the passage of the contraction wave. Each end of the muscle is connected with a lever arranged to write on a moving surface. The electrodes are connected with a commutator for changing the direction of the current, and this with the circuit of a battery, in which a make and break key is placed. A rheocord, for varying the strength of the current passed through the muscle, is placed between it and the commutator.

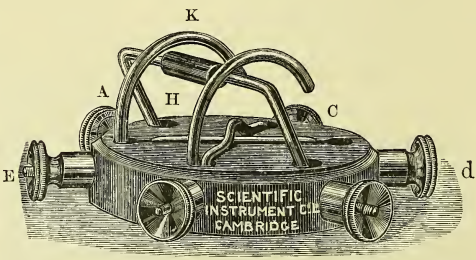


Fig. 107.—Pohl's Commutator.

[A *Pohl's commutator*, for reversing the direction of the current, is shown in the accompanying figure. The binding screws, A and B, are connected with the battery, C and d with the electrodes. With the bar H (a non-conductor) in its present position, the current entering at A will pass along to the mercury cup E, then by the cross wire to d, through the electrodes to C, then to F, and through B back to the battery. But if H be tilted so that its

other two curved bars rest in the mercury cups C and d, while it has become disconnected with E and F, the current entering at A passes by K to C, through the electrodes to d, and again by B back to the battery. That is to say, that in the first instance the current passes through the electrodes from C to d, in the second from d to C, so that we may make the current either descend or ascend; that is, we may reverse the relative position of the anodal and cathodal points of stimulation of a muscle or nerve.

But Pohl's commutator may be used for another purpose. If it is desired to send a current alternately through two preparations, or different parts of the same preparation, *e.g.*, through a nerve and then through its muscle directly, it may be arranged as follows: the

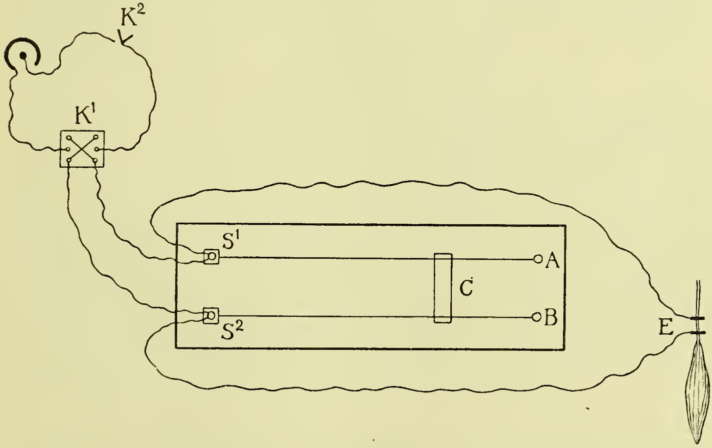


Fig. 108.—Rheocord and Pohl's Commutator Arranged to Vary the Strength and Direction of a Current through a Muscle.

cross wires are removed, the mercury cups filled as before, A and B connected with the battery, C and d with one pair of electrodes, *e.g.*, those for the muscle, and E and F with another, *e.g.*, those for the nerve. When the cross-bar H is tilted so that the curved ends rest in the cups E and F, the current will pass through the nerve; when they rest in C and d the current is sent through the muscle.

A *rheocord* is shown in Fig. 108. The principle is that of a deriving circuit being introduced in addition to the main one, so that the current is divided. The amount passing through the stimulating circuit is directly proportional to the resistance in the

deriving circuit, and this is varied by a movable contact running upon two wires. When the contact C is moved towards the binding screws S^1 and S^2, more and more of the current passes through the deriving circuit and less through the stimulating; but when C is moved towards A and B the reverse is the case. K^1 represents the commutator and K^2 the key in the battery circuit.]

If a current be now sent through the muscle by closing the battery circuit, it will be found that the half of the muscle connected with the zinc of the battery, *i.e.*, that connected with the positive element by the negative pole, the cathodal part of the muscle, contracts first, and then the anodal part. Both levers rise, and the difference in time is ascertained by measuring the latent periods of each curve, with a view to which a time-signal has been placed in the primary circuit. On opening the circuit the lever connected with the anodal extremity of the muscle moves first, the difference in time as before being shown by the latent periods.

If the direction of the current be now reversed the previous cathodal area contracts last on closing, as it has now become anodal, and the anodal area last on opening, as it has now become cathodal. By means of the rheocord the difference in strength between the anodal and cathodal stimulation may be shown. The movable contact is pushed along the wires towards S^1 and S^2 till a point is reached at which so little current passes through the stimulating circuit that contraction is only induced on closure of the key, K^2. Also on moving the contact in the opposite direction, and at the same time increasing the battery strength, a point is reached where galvanotonus is produced, appearing first at closure.

Chemical, Thermal, and Mechanical Stimulation of Muscle and Nerve.

A solution of common salt will act as a chemical stimulus, a cut or nip with the forceps as a mechanical one, a hot wire or rapid cooling as a thermal stimulus. All these methods are very irregular and uncertain in their action, often producing irregular tetanic contractions.

Direct Stimulation of Muscle by Non-Nervous Stimuli.

That muscle is directly excitable is readily shown as follows:—(1) The ends of a frog's sartorius, which contain no nerves, respond to direct stimulation. (2) Ammonia and some other substances

act upon muscle as a stimulus, but not upon nerve. (3) If the motor nerve to a muscle be divided, and degeneration of the nerve allowed to take place so that stimulation of the trunk gives no contraction, the muscle will still respond to direct stimuli. (4) Effect of curara, by which the motor terminations of the nerve are paralysed, and direct stimulation of the muscle fibre leads to contraction (page 92).

The Contraction of Muscle.

To obtain a record of a simple contraction, a revolving drum bearing blackened paper, a nerve-muscle preparation, a moist chamber or a crank myograph to hold the muscle, an induction

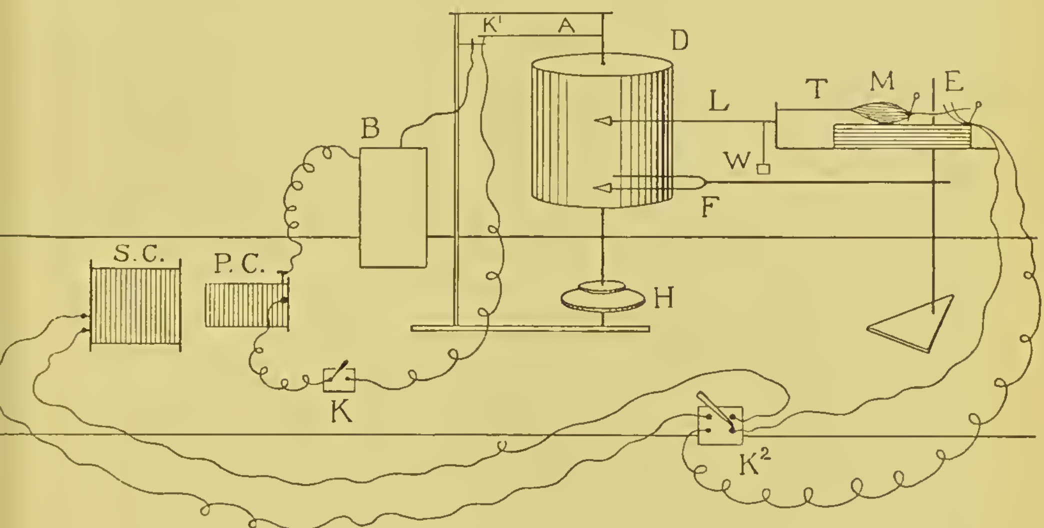


Fig. 109.—Apparatus for Recording Simple Twitch of Muscle.

machine and battery, wires, electrodes, keys, and a tuning-fork are required. They are connected as shown in Fig. 109. It will be observed that the make and break (in this case break) key, K^1, in the primary circuit is placed in relation to a metallic arm, A, projecting from the axial rod of the drum, D, which by its revolution opens the key and breaks the current. This method of stimulation is necessitated in order that the exact time at which the shock is sent into the nerve may be recorded. As usual, the secondary circuit is short-circuited by the key K^2. The figure shows the gastrocnemius muscle, M, placed upon the crank myograph, to which it is fixed at its proximal end by a pin, with the sciatic

nerve belonging to it resting on the electrodes, E. The tendo Achillis of the muscle is connected by a thread, T, with the vertical rod of the crank, while from the horizontal projects the writing-lever, L, to which a paper or platinum point is attached. F is a tuning-fork for recording vibrations in parts of a second.

The writing-point of the muscle lever is adjusted to touch the drum surface, while that of the tuning-fork is not in contact. The drum is then slowly turned by the hand, from right to left, till the point is reached at which the revolving arm, A, opens the circuit by striking the key, K^1. The muscle twitches, and the writing-point of its lever describes a vertical line on the blackened surface. The drum is now rotated through half a revolution, the key, K^1, again closed, the writing-point of the tuning-fork brought into position upon the blackened paper below that of the muscle lever, and the drum allowed to rotate at an appropriate speed. As the circuit is again opened, and the current broken as before by the revolving arm, a shock is sent along the nerve into the muscle, and the latter, by its contraction, raises the lever, and thus describes the muscle curve. At the same time the vibrations of the tuning-fork have been recorded. The drum is now stopped, the tuning-fork removed, the short-circuiting key, K^2, closed, and the writing-point of the muscle lever accurately applied to the base line. The drum is then again rotated by hand and an abscissa obtained. The rotation is continued till the point is reached at which the stimulus was thrown in, when the lever is gently depressed, so as to cut the time record ; and other arcs are also taken—one at the point where the curve leaves the abscissal line ; one so as to cut the curve at its highest point ; and a third where it reaches the abscissa again. Each of these arcs should cut the curve and the time-tracing too.

Such a curve is shown in Fig. 110, where *b*, *c*, *d* is the muscle curve, *a*, *b*, *d* the abscissal line, *a'*, *b'*, *c'*, *d'* the time-tracing.

It may be noted in passing that the distance from *b* to *d*, *i.e.*, from the point at which the curve leaves the abscissal line to the point at which it reaches it again, depends upon the speed at which the drum rotates. If slowly, the points will be nearer together ; if quickly, further apart. The curve shows three subdivisions :—(1) the *latent period*, extending from the point *a*, at which the stimulus was thrown in, to *b*, where the curve first leaves the abscissal line, and preceding the actual contraction of the muscle. In the frog it occupies from ·003 to ·008 seconds ; but it cannot be accurately measured by the above method. The latent period here obviously represents the time occupied by the changes going on in the muscle preparatory to contraction, and

also the time spent in the passage of the nerve impulse along the length of the nerve. (2) The *period of contraction;* at first rapid, where the curve is convex to the abscissa, and afterwards slower, where it is concave: this portion of the curve extends from *b* to *c*. (3) The *period of relaxation*, from *c* to *d*, showing the same phases; first, rapid relaxation where the curve is concave to the abscissa, and afterwards slower where it is convex. As the tuning-fork vibrated at the rate of 200 per second, the relative length of these three periods in the above tracing is as follows:—latent period, $\frac{1}{200}$ seconds; period of contraction, $\frac{11}{200}$ seconds; period of relaxation, $\frac{14}{200}$ seconds. These added together give the total time for this twitch as $\frac{26}{200}$ seconds, or ·13 seconds.

The oscillations of the line drawn by the lever after the contraction is over are largely mechanical, and result, for the most part, from the inertia of the weight and the elasticity of the muscle.

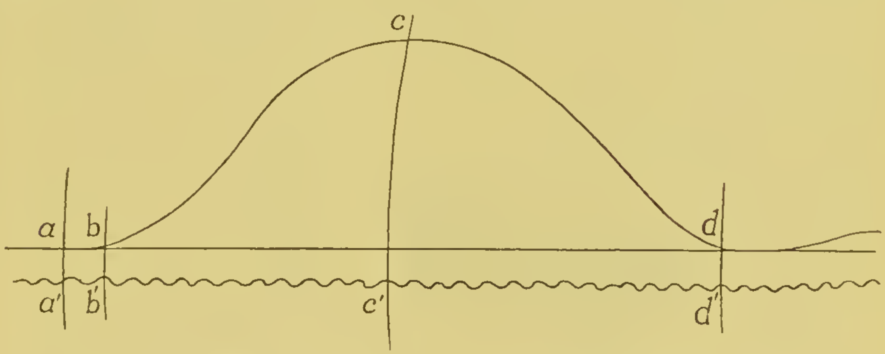


Fig. 110.—Simple Muscle Curve, with Time-Tracing.

Contraction remainder.—When a muscle has been strongly stimulated, or is fatigued, it may not regain its original length for some time after the twitch is over, unless it is sufficiently weighted; and this delay has been termed "the contraction remainder."

In obtaining a tracing of a simple muscular contraction, instead of a revolving drum, the *pendulum myograph* may be used, the principle of which is shown in the accompanying diagram. It consists of a pendulum frame, B, carrying a piece of plated glass, A, to which a sheet of smoked paper is clamped, and which swings between the two catches, *b* and *b'*. As in the case of the revolving drum, the pendulum itself breaks the primary circuit in its excursion, thus enabling the point at which the current is sent in to be recorded. The writing-point of the muscle lever is adjusted lightly against the smoked surface, the pendulum being held by the catch spring, *b*, on the right. It is then released from the

spring and guided carefully by hand until the point of contact between a' and c, the upright of the make and break key, is reached. The lever is now slightly raised, and a short vertical line thus drawn upon the blackened surface, indicating the point at which the shock will be sent in. The pendulum is then carefully returned to its former position, again released, and allowed to swing to the left, where it is detained by the catch spring, b'. In its excursion it opens the key, e, in the primary circuit, a shock is sent into the muscle, and its curve recorded. The pendulum is then again placed on the right side and (the key being left open) allowed to swing again, so that an abscissal line may be drawn, and the time recorded by the tuning-fork beneath it.

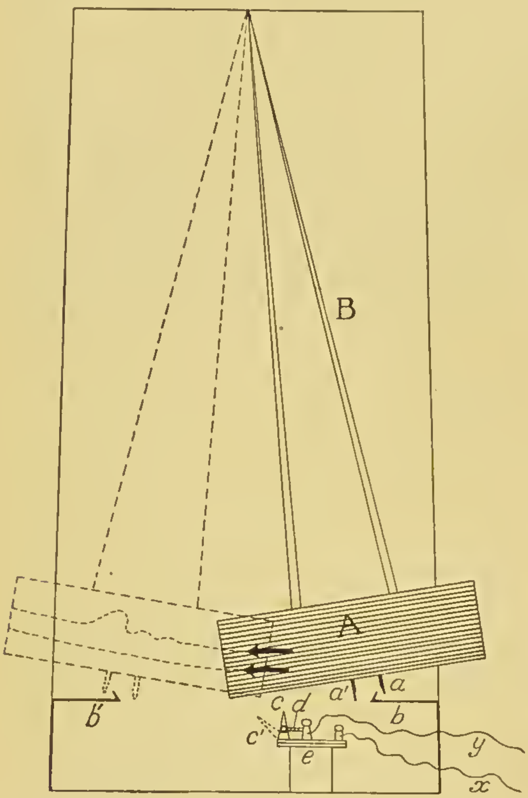


Fig. 111.—Principle of Pendulum Myograph.

A *chronograph* is frequently used to record the time, as a tuning-fork is in many ways inconvenient, and by itself soon ceases to vibrate. The chronograph consists of an electro-magnet and a movable armature, to which a writing-point is affixed. As the current is made and broken by the tuning-fork in the same circuit,

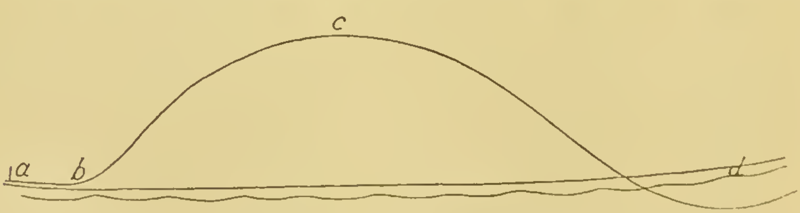


Fig. 112.—Simple Twitch of Muscle, recorded by Pendulum Myograph.

the coils of the chronograph are alternately magnetised and demagnetised, the armature being alternately attracted and released. The tuning-fork is kept vibrating by means of an electro-magnet, one of its prongs alternately making and breaking the current as it touches and recedes from a platinum wire.

A *spring myograph* is also in use, in which a plate carrying smoked paper is carried along parallel metal bars by a spring, and breaks the current during its excursion. In some instruments the plane of the plate is vertical, in others horizontal.

The muscle not only *shortens* during contraction, but *thickens*, and this may be demonstrated by placing a lever upon its belly, when a curve may be obtained during contraction very similar to that already described. The thickening of a muscle during contraction in the human body is readily studied with the aid of the *myographic forceps*, connected with a writing-lever by tubing and a tambour; the lever rising and falling as the shock enters and leaves the muscle. The forceps may be readily applied to the short adductor muscles of the thumb.

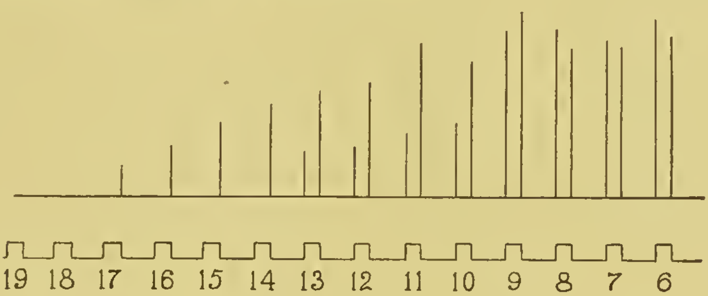


Fig. 113.—Record of Contractions of Muscle with Different Strengths of Stimuli. The Numbers Correspond with Scale of Secondary Coil.

Various conditions influence the curve of a simple contraction:—

1. The **stimulus.**—Within certain limits the contraction of the muscle varies with the strength of the stimulus. On starting with the coils far removed from each other, and gradually decreasing the distance, stimulation will be found to occur first at the break shock; and this is termed the *minimal stimulus*, and the resulting contraction is also called *minimal*. The minimal stimulus in the accompanying Fig. occurred at 17 *c.m.* of the scale. After the point 9 on the scale no higher line was traced, and this is termed the *maximal stimulus*, and the contraction the *maximal contraction*. All stimuli to the left of 17 are *subminimal*, and all between 17 and 9 *submaximal*. It will be seen that a contraction at make

first occurred at 13. The break stimuli to the right of 9 are *supermaximal.*

2. The **resistance to be overcome.**—At first sight it might be expected that the contraction of the muscle, *i.e.*, the number of units of height through which it will lift a load, would be inversely proportional to the mass of the latter. But this is not the case; an increase of weight (within certain limits), by increasing the tension, may enable the muscle to lift the weight to even a greater height. We have said within certain limits, for though a certain tension is favourable to a muscle's power of contraction, a point is ultimately reached at which the strongest stimulus fails to enable the muscle to lift the load at all. But though a load is favourable to eliciting the greatest degree of contraction in a muscle, it interferes somewhat in the production of a curve showing a perfectly normal muscle contraction; for the simple reason that the inertia of the weight prevents its following accurately the movements of the muscle. Thus, as the latter raises the weight, this acquires a certain amount of kinetic energy of its own which carries it upwards, and this acceleration continuing relieves the muscle of some of the tension upon it, so that its elasticity produces a shortening in addition to that due to the contraction. Again, in relaxation the tension is relieved in the first part, as the weight does not follow the relaxation quickly enough; but subsequently, as this slows, it is overtaken by the weight, with the result of an increase of tension and a drawing out of the muscle beyond its initial length. When this downward acceleration of the load is stopped, tension comes into play and raises the load again, and this may be repeated until after one or two further oscillations equilibrium is attained.

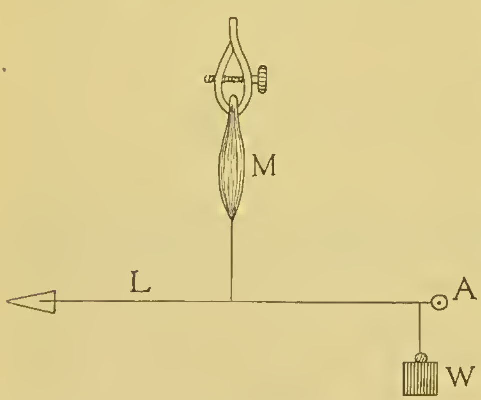


Fig. 114.—Principle of Isotonic Method.

With a view to being able to work with a load attached to a muscle, and at the same time to avoid the disadvantages of the acceleration referred to, and the consequent production of different degrees of tension in the muscle at different stages of the contraction, it is usual to employ special methods of loading, of which the

isotonic is one. In the accompanying figure the weight is shown applied at some distance from the point at which the thread from the muscle is attached to the lever, and near to the axis. It will be obvious that here the tension on the muscle will be much less than if the weight were attached immediately beneath it, and also much more constant, inasmuch as the excursion of the weight is so much the less.

By the *isometric* method the change of tension is recorded, and the change in the length excluded. Here the muscle pulls upon a lever, C A, with its axis at A. A B is a stiff spring, resting upon a knife edge at B. The muscle in contracting tends to raise the lever, C A, but this is prevented by the spring, A B. The small movement produced in spite of the spring is, however, greatly exaggerated by the lever, and so an isotonic curve showing the tension, but not the shortening, is obtained.

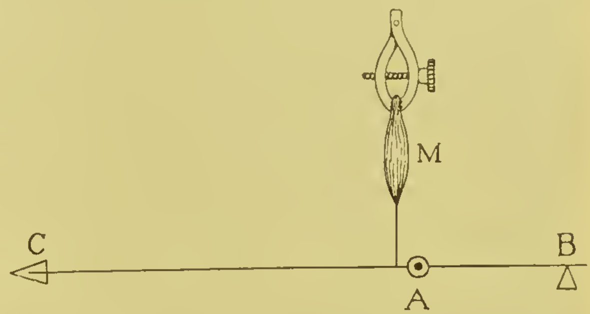


Fig. 115.—Principle of Isometric Method.

If, after obtaining a tracing in this way, the muscle be removed and a pulley be substituted, through which the thread attached to the lever is drawn, and a weight be attached to the end of the thread, an abscissal line may be drawn showing the tension value of the weight. An additional weight will give another abscissa, and so on. In this way the value of the tension of the muscle on the spring at different points during its contraction may be obtained.

3. **Fatigue.**—If an excised muscle be repeatedly stimulated to contraction at regular intervals, it is found that the height of the tracings becomes at first slightly and regularly increased, to be followed by a more marked and progressive diminution. The curve is also very much extended, owing to the lengthening of the period of relaxation, while that of shortening is not very much affected. When the tracing is taken on a rapidly-revolving drum, the stimulation being thrown in always at the same point, a "fatigue curve," such as is shown in Fig. 116, is obtained. In such a tracing one or more revolutions may take place in the later stages of fatigue before relaxation is complete and the style

comes back to the abscissa. Fig. 117 shows a "stair-case" tracing, giving the relative height of the contraction before and after the maximum is attained, but not the lengthening of the period of relaxation. The latent period is increased in fatigue.

Fatigue in an isolated muscle is no doubt due to the using up of the material necessary for contraction at a quicker rate than it can be supplied and the presence and accumulation of the products of the working muscle. These latter may be represented by sarco-lactic acid, acid sodium phosphate, and CO_2. If they are washed

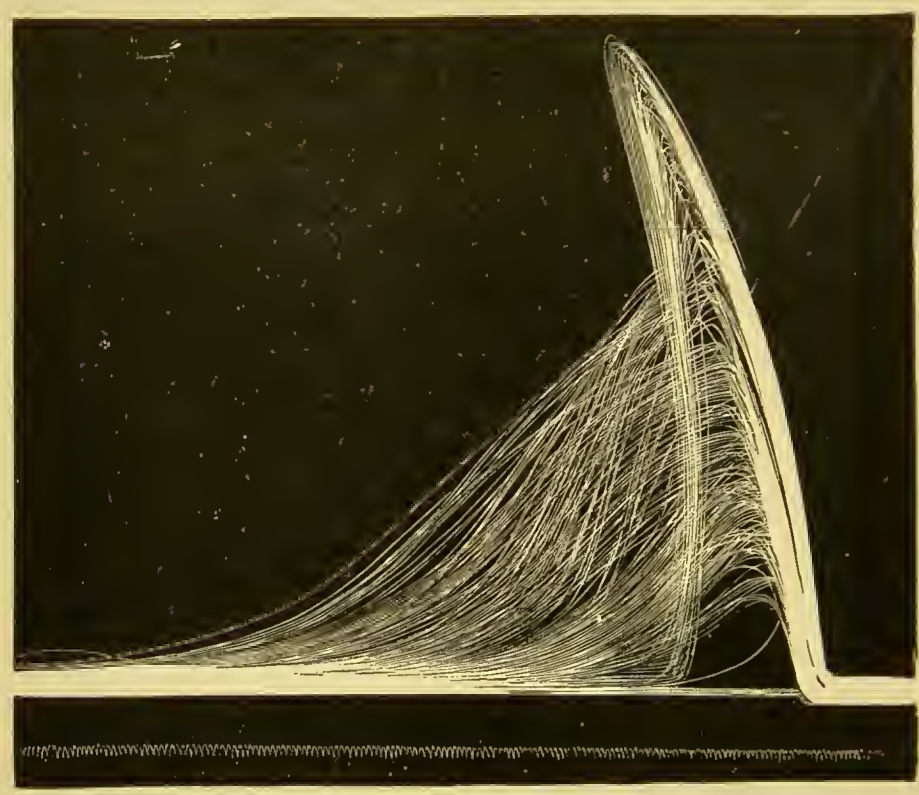


Fig. 116.—Fatigue Curve of Skeletal Muscle (Gastrocnemius of Frog). Indirect Stimulation.

out from an exhausted muscle by normal saline, it again becomes capable of evolving energy; and the injection of oxidising agents, such as arterial blood, has a similar effect. Fatigue may also be induced by the injection of extract of meat, phosphoric acid, or acid sodium phosphate. The unexcised muscle is not nearly so easily fatigued as the excised one, but the phenomena of fatigue are the same. The restorative effect of massage upon exhausted

muscle is probably due to the mechanical "washing out" of the products of muscular contraction.

The nervous fatigue after voluntary exertion is chiefly central. The muscles will respond to electrical stimuli, applied directly or through their nerve trunk, when voluntary movement cannot be made. In the excised fatigued muscle the exhaustion is apparently in the nerve endings, as the muscle can be stimulated directly after indirect stimulation fails; though the nerve trunk still exhibits negative variation, and will transmit impulses. For if two nerve muscle preparations be taken, the nerves laid upon the stimulating electrodes, and a drop of alcohol and ether in water be placed on one nerve, between the electrodes and the muscle, on the tetanising current being sent in, the anæsthetised portion of the one nerve acts as a block and its muscle is unaffected, while the muscle of the other nerve contracts, and is in time exhausted. If the solution of alcohol and ether be now washed off with normal saline, the block on this nerve is removed and its muscle becomes tetanised, showing that the nerve trunk itself is not affected.

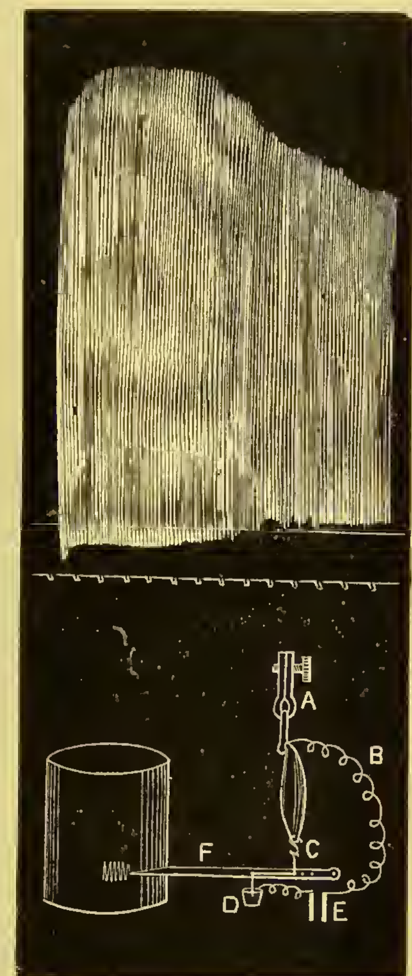


Fig. 117.—Fatigue Curve of Muscle (Frog's Gastrocnemius) and Apparatus with which it was obtained.

A, Clamp holding femur; *C*, attachment of muscle to lever *F*; the wire of the hook *C* is continued along lever and connected with a needle which just dips into mercury cup *D*; one wire from battery *E* dips permanently into the mercury, the other, *B*, passes to the upper end of the muscle. Each time the needle touches the mercury, the muscle is stimulated automatically.

In voluntary muscular fatigue it seems, therefore, that exhaustion takes place at the fountain-head—the motor nerve cells of the cortex cerebri; and this is accompanied by the using up of the substances required for contraction, and the loading up of the

muscle itself with the products of its contraction; whereby its activity is hindered, the nerve endings being first affected. The

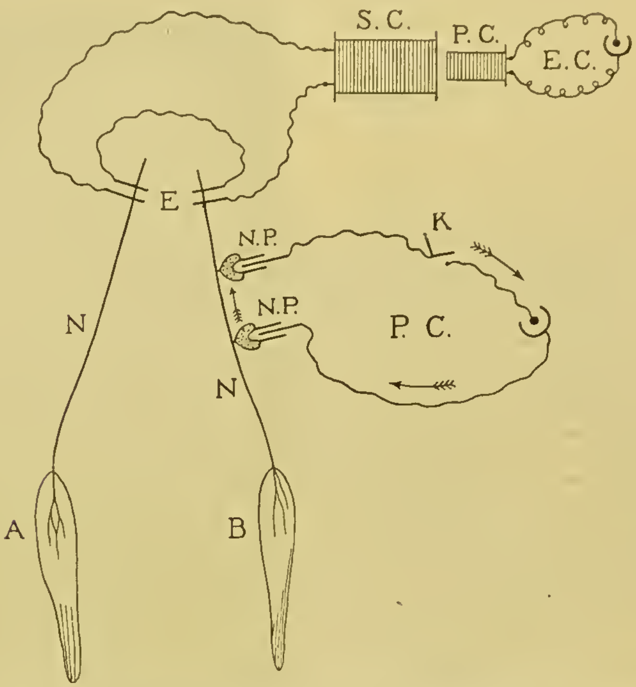


Fig. 118.—APPARATUS FOR SHOWING ABSENCE OF FATIGUE IN MEDULLATED NERVE FIBRES.

E.C., Exciting current; *P.C.*, polarising current, which acts as a block in the same way as a drop of alcohol and ether in water. On sending the exciting current into both nerves, muscle *A* becomes first excited and then fatigued; if the polarising current *P.C.* be now broken, muscle *B* passes through the same phenomena, showing that the fatigue has not affected the nerve trunk, as the exciting current passed through both nerves.

nerve fibre between the central nerve cell and the muscle itself seems to be the least affected part of the chain.

Fig. 119.—VERATRIA CURVE (FROG'S GASTROCNEMIUS).

4. The **effect of drugs—veratria.**—The action of veratria is particularly interesting. Under its influence the muscle contracts as usual, but the period of relaxation is greatly prolonged, even more so than in the case of fatigue.

5. The **individuality of the muscle.**—In different animals the rate of muscular contraction varies, and this is also the case in the muscles of the same animal. The red muscles of the rabbit contract more slowly than the white, and the hyoglossus of the frog more slowly than the gastrocnemius. The muscles of the tortoise are proverbially slow in action.

Summation of stimuli and tetanus.—When a muscle is subjected to a single induction shock such a tracing as already

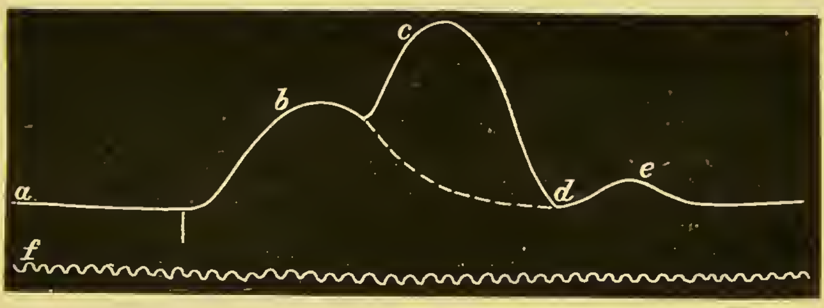


Fig. 120.—Tracing of a Double Muscle Curve.

While the muscle was engaged in the first contraction a second shock was sent in at such a time that the secondary contraction began just as the first was beginning to decline; *b*, first contraction; *c*, *d*, second contraction; *f*, time-tracing.

described (page 107) may be obtained; and succeeding shocks give rise to similar curves until fatigue supervenes, when the curve becomes altered in character as already indicated. We have now to study the result when these succeeding shocks are sent in so rapidly that the lever has not time to return to the abscissal line after any one of them before its successor is thrown in; and first we may enquire into the result of sending two shocks into a muscle in rapid succession. In this case the second shock may be thrown in either before the latent period of the first is over or immediately after. If before, then, if the stimulus employed be a maximal one, only one curve is obtained, which is similar to that which would have resulted from the first shock alone; but if the shocks are less than maximal, the result of the second shock is to raise the lever higher than would have been

the case if one shock alone had been sent in. That is to say, we have here an instance of the *summation* or addition of *stimuli*, the effect of the second shock being superadded to that of the first. At the same time the curve is a single one, precisely resembling such a one as would be obtained by a single shock of sufficient strength.

If, however, the second shock is sent in after the latent period is over, *e.g.*, during the period of shortening, let us say towards its close, the tracing clearly reveals the compound nature of the stimulus, the second curve starting from the top or nearly so of

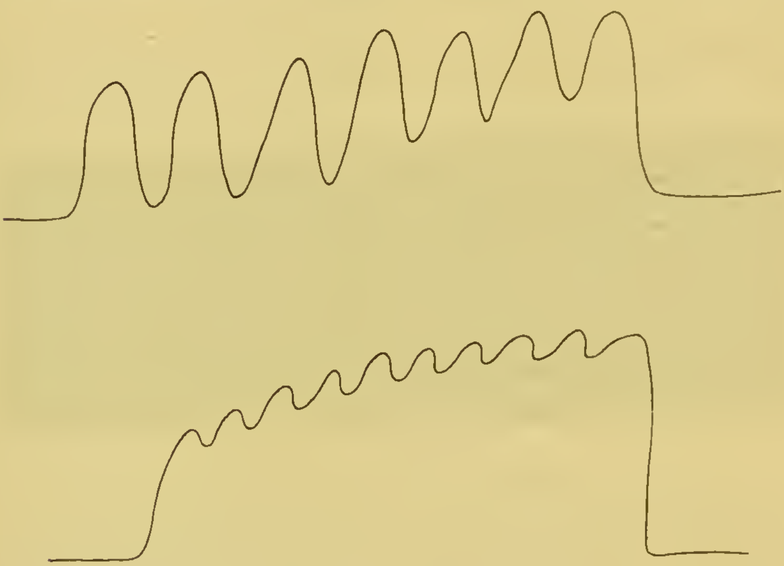


Fig. 121.—Genesis of Tetanus.

Single induction shocks repeated comparatively slowly.

the first; and the height of the compound curve is much greater than that of the single one would have been, even if the stimulus has been maximal. When a succession of shocks is sent into a muscle, the result is virtually the same, a third curve being superimposed upon the second, and a fourth on the third, and so on until a maximum of shortening is obtained, after which the lever describes a somewhat horizontal line, upon which secondary wavelets appear, indicating the shocks as they are sent in. As soon as the stimulation is withdrawn the lever drops, at first rapidly and then more slowly, till it reaches the abscissal line.

But if the stimuli are sent in with sufficient rapidity, the component parts of the curve cannot be distinguished, and we

have as the result an apparently simple tracing in which all the secondary curves are fused. This is the condition of *complete tetanus*, which will be seen to be a *compound contraction*, made up of a number of successive and superimposed twitches fused together. When the shocks are sent in at sufficient intervals to allow the component curves of the tracing to be distinguished, the condition is called *incomplete tetanus*, and by separating the shocks still more we may pass from the summation of stimuli back to entirely separate simple curves. Incomplete

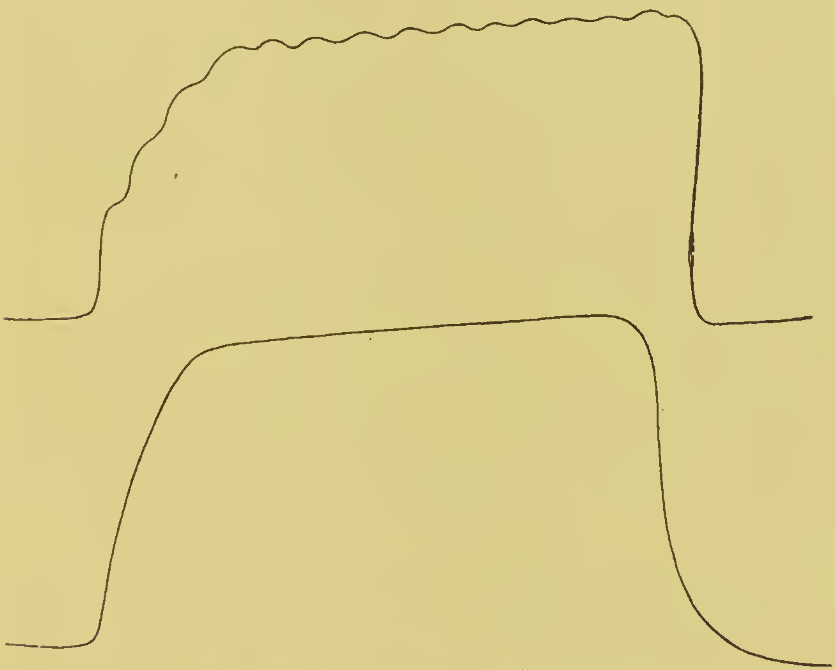


Fig. 122.—GENESIS OF TETANUS.

The last tracing shows complete tetanus produced by the use of Neef's magnetic interrupter.

tetanus begins when these simple curves are brought so close together that each starts from some part of the previous one, and not from the abscissal line.

This summation of stimuli, illustrated here by the tetanisation of muscle, occurs in connection with any irritable tissue. The effect of an irritant is greater if it be applied before the effect of the previous application has passed off. The effects of several stimuli thus accumulate and lead to a discharge of energy greater than any individual one would have produced. It is upon this principle that a "policy of pin-pricks" is often effective, the effect of the

oft-repeated irritation accumulating until the result in the direction desired takes place. The reiteration of the same argument in a daily paper is continued in reliance on the same law that impressions repeated sufficiently frequently at short intervals will have a cumulative effect if they overlap—that is, if the second impression is made before the first is obliterated. The application of a street beggar for alms, though often futile at first, if persistently repeated may produce, by summation of stimuli, a sufficiently powerful effect on the nerve centres to find expression in the discharge of a small coin or in some other way.

Inasmuch as the muscles of different animals have a different contraction speed, it follows that the number of stimuli per second required to produce tetanus will vary in different cases. If the contraction and relaxation is rapid, a larger number of shocks will be required to insure that relaxation is not complete, and that superposition of the curves takes place. The muscles of insects require 300 stimuli per second for complete tetanus, those of birds 100, of man 40, and of the tortoise 3.

Fatigue also, inasmuch as it lengthens the period of relaxation, renders a muscle much more readily tetanisable.

But continuous contraction may take place without the muscle being tetanised, as already mentioned in the case of galvanotonus; and the slow tonic contraction of the circular non-striped muscle of the intestine is not an interrupted but a simple one, contrasting markedly in time with the simple twitch of voluntary muscle. The contraction of the muscular fibres of the heart is also simple, and occupies an intermediate position between these two.

The **rate of transmission of the wave** of simple contraction may be ascertained by arranging levers, placed as far apart as possible upon a muscle, to write, one above the other, on a smoked drum, and then stimulating one end of the muscle. A time record is taken with a tuning-fork beneath the tracing, and the distance between the points where the two levers rise from the abscissal line divided by the time gives the rate of wave progression.

In **voluntary contraction** each muscle fibre is stimulated about its centre through the nerve fibre supplying it.

When a muscle is thrown into tetanus by stimulating its nerve with an interrupted current, it is found that the number of muscular vibrations corresponds exactly with that of the interrupter. When, however, the motor area in the brain presiding over the muscles, the corona radiata, or the spinal cord is stimulated, the rate of vibrations in the muscles tetanised has been observed to remain the same, whatever the rate of the interrupter has been; and from this it is concluded that this rate (about 10–12 per second)

represents the usual number of discharges per second from the motor nerve cells.

The *muscular sound* produced in a contracting muscle (readily heard in the masseters if the jaw be clenched in the stillness of the night) has been largely relied upon as evidence of the compound nature of a voluntary contraction. The note heard, however, possesses 36–40 vibrations per second, this being the same as the resonance note of the ear itself, and may be the first overtone of the fundamental note with vibrations at the rate of 19·5 per second; and Helmholtz found that reeds (attached to muscle) vibrating at the rate of 19·5 times per second were more affected by muscular contraction than those whose vibration speed was greater or less. There has been a good deal of difference of opinion as to how far the pitch of the note given out by a contracting muscle may be taken as an indication of the number of contractions which go to make up the tetanus, and it may be that the muscle sound is dependent on alterations of tension in the muscle during contraction, rather than on a succession of vibrations corresponding with a definite number of single contractions per second. However, the fact that the note is similar in all the voluntary muscles of the body would seem to show that the number of single contractions per second is tolerably uniform, and this number, from vibrations on myographic tracings and other evidence, is generally put at 10 or 12 per second; so that voluntary contraction (except when instantaneous) may be regarded as an incomplete tetanus due to the discharge of 10–12 impulses per second from the motor cells in the brain.

The **work done by a muscle,** as by the body generally, is both external and internal. The external work is estimated by the product of the weight lifted and the height through which it is raised. Inasmuch as stretching a muscle affects its metabolism and functional activity, it is usual in making experiments in work done to "after-load" it, by which the weight comes upon the muscle only at the moment of contraction; and this is done by suitably supporting the weight and lever. The *absolute muscular force* of a muscle is represented by the weight required to prevent it shortening, which is at the same time not sufficient to cause it to stretch. This force decreases as the muscle contracts, a smaller and smaller weight being required, until at the end of contraction it is represented by zero. The muscles of the animal body are so arranged that they work in recognition of this principle, for the greater amount of work to be done is usually at the commencement of contraction, and it decreases progressively towards the end.

The amount of work done by a muscle will depend on several factors—(1) The *stimulus.*—The greater the stimulus the greater the contraction, within certain limits, and an interrupted current produces a greater shortening than a single induction shock. (2) The *load.*—A certain weight is necessary to call forth the greatest amount of work in any particular muscle: that is to say, a muscle loaded and stimulated to contraction, may, on the load being doubled, raise it the same height, or even a greater one, though of course this is not continued indefinitely, a point being reached when even the strongest stimulus does not cause it to lift a load. (3) The *size* and *length* of the muscle.—The longer the muscle the more shortening can take place, and the thicker it is the greater weight it can raise. Thus the work done by a muscle varies with its mass, taking the specific gravity as the same.

The Chemistry of Muscle.

Rigor mortis—chemical changes in contraction.—When a muscle is separated from the body, or in the body after general death, it loses its irritability, and passes into the condition of *rigor mortis.* In this state its translucency gives way to opacity, its suppleness to rigidity, and its extensibility and elasticity are largely diminished. Rigor mortis usually supervenes in from one to four or five hours after death, though it may come on more quickly—a high temperature and fatigue facilitate its onset. It commences in the jaws and neck, thence passes to the arms and thence to the legs, lasting from one to three days, and disappears in the same order. When it has once supervened, irritability cannot be restored.

To make plain the chemical changes which occur it will be convenient to study first the composition of a dead muscle (one which has already become rigid) and then return to the considera-tion of the living muscle. If a dead muscle be minced and washed with water until the washings cease to show any traces of proteid, the greater part of the muscle is still left. If this be now extract-ed with neutral salt (10% solution of ammonium chloride is the best), an opalescent fluid is the result, which yields a flocculent and copious precipitate when poured into excess of water. The pre-cipitate is *myosin*, the globulin of muscle, giving the ordinary proteid reactions, and being precipitated from its solution by saturation with neutral salt. It is also precipitated by alcohol and coagulated by a temperature of 56°C. It is readily converted to

acid-albumin by the action of weak hydrochloric acid, the resulting jelly being known as *syntonin*.

The other constituents of muscle, after the removal of the myosin by a solution of neutral salt, consist of the gelatine-yielding portions of the tissue, nuclei, &c., extractives, fats, carbohydrates, salts, and water. In a tabulated form the composition of dead muscle may be given as follows:—

	Water	75 per cent.
	Proteids	20 "
	Fats	2 "
Extractives,	Kreatin, Xanthin, Hypoxanthin	2 "
Carbohydrates,	Glycogen, Sarcolactic Acid, Inosite	

Salts, chiefly carbonate and phosphate of potassium, less than 1 per cent.

The reaction of muscle which has undergone rigor mortis is distinctly acid, due to the presence of CO_2 and sarcolactic acid. The increased evolution of CO_2 with the onset of rigor is not, however, in a separated muscle due to increased oxidation; for no oxygen can be drawn from such a muscle, and even when working in an oxygen-free atmosphere the evolution of carbonic acid with the onset of rigor takes place. Moreover, in a muscle supplied with blood the amount of CO_2 evolved is in excess of the amount of oxygen absorbed from the blood, so that the CO_2 is probably set free from some previously-formed complex substance whose carbon has been oxidised at an earlier date.

As there is a fairly constant relation between the amount of rigidity, the acidity, and the amount of CO_2 evolved, it would appear as if the production of these last were intimately associated with the coagulation of the hypothetical myosinogen of the living muscle, to which we now turn.

If living frozen muscle be minced and rubbed up with four times its bulk of snow containing 1 per cent. of common salt, a solution of *muscle plasma* is obtained, which is opalescent and filters with difficulty. If allowed to return to the ordinary temperature it quickly sets, first to a jelly and then clots, the clot expressing a serum, as in the coagulation of blood; but here the clot is granular and flocculent, instead of firm and fibrillar. The change, as in the production of fibrin, is probably due to a ferment.

The serum contains serum-albumin and globulin, extractives, salts, histohæmatin and a little hæmoglobin. The clot is composed of myosin, and this coagulation of the muscle plasma, after separation from the living muscle, probably represents the change that takes place with the onset of rigor mortis in a muscle after general death; the rigidity, opacity, and loss of elasticity all being due to the fluid plasma of the muscle setting to a jelly.

Whereas the reaction of living muscle is neutral and amphichroic—that is, turns red litmus blue, and blue red—the reaction of dead muscle, as we have seen, is decidedly acid, and in this way offers a marked contrast to the coagulation of blood, in which little change in reaction occurs.

In many ways the phenomena during contraction resemble those of rigor mortis. The reaction becomes acid from the presence of sarcolactic acid, and there is evolved a considerable amount of CO_2, which, as in the case of rigor, does not require the presence of oxygen, either in the muscle or in the atmosphere in which it works, as in the case of a frog's muscle acting in nitrogen; and though in a muscle supplied with blood, more oxygen is consumed during contraction, yet the amount falls short of the CO_2 given off. In contraction, however, as opposed to rigor, no myosin is formed, and the extensibility and elasticity of the muscle is even increased rather than lessened.

The nitrogenous output of a muscle does not appear to be increased by contraction; there is no evidence of nitrogenous waste, though the sarcolactic acid is probably produced from proteids by the action of a ferment.

The glycogen distinctly diminishes during contraction, but accumulates in a resting muscle.

During rest the muscle takes up proteid, carbohydrate, fats, salts, and water from the blood, and builds them up into its living substance, and continually gives off certain products, of which sarcolactic acid, kreatin, and CO_2 may be taken as examples. The energy required for muscular contraction can be obtained from any of the three great food constituents—proteids, carbohydrates, and fats—but this question—the chemical source of muscular energy—will be considered with "Metabolism."

Production of heat during contraction of muscle.—When a muscle contracts, certain chemical changes take place which result in a discharge of energy, part of which appears in the form of work done and part as heat. This production of heat is constantly going on, even in a resting muscle, as the result of its metabolism, but it is largely increased during functional

activity. The rise in temperature may be roughly estimated by plunging a mercurial thermometer into or between the muscles, and noting the difference before and after tetanus has been induced. But for the purpose of estimating slight variations accurately a more delicate apparatus is required—a *thermopile*, which, when heated, however slightly, gives rise to a current which deflects the needle of a galvanometer. The apparatus consists of two junctions or "thermo-elements," each consisting of two different metals (German silver and iron, copper and tin, or antimony and bismuth). The two similar free metals are united by wire, so that the whole forms part of a closed circuit, part of which is arranged in coils round the magnet of the galvanometer. This has been rendered nearly astatic by the introduction of another magnet to oppose and nearly neutralise the earth's influence; the nearer the galvanometer magnet is to being astatic, the more sensitive is it to the currents passing through the wires that surround it. To it is attached a small mirror which moves with it and casts a reflected spot of light upon a scale; when no current is passing and the magnet is stationary, the spot of light should be in the middle of the scale at zero. If now one thermo-element be placed in the thigh muscles of a frog's leg and the other into the muscles of the other leg, the temperature of the two sets of muscles being the same, no current will pass, as the two opposing currents are equal in strength; but if the muscles of one leg be tetanised, additional heat is evolved, the current in that thermo-element is increased, and the galvanometer magnet with its mirror is deflected, the spot of light moving away from zero. So many degrees on the scale correspond to such a difference in

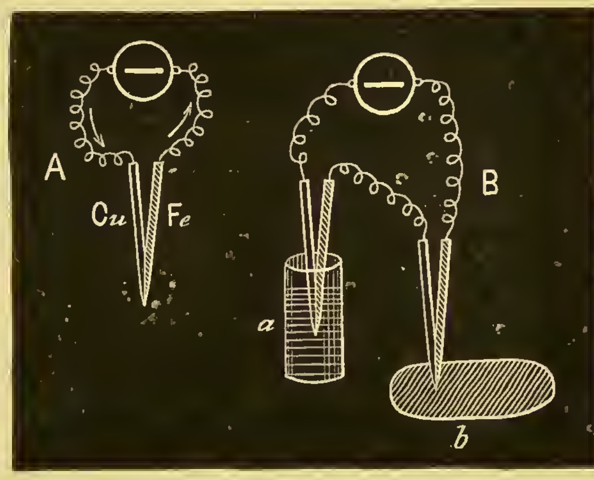


Fig. 123.

A, Single copper-iron thermo-electric couple; *B*, two pairs, one inserted into tissue *b*, the other dipping into water in beaker *a*. When the galvanometer shows no deflection the temperature of the water is the same as that of the tissue; so by adjusting the temperature of the water till no deflection is observable the temperature of the tissue may be ascertained. (In *B*, by an oversight, the wires are shown joining different instead of similar metals.)

temperature, and it is obvious that before we can make any profitable use of the method, this value must be determined. This is readily done by placing each thermo-element in a vessel containing oil, the one bath being 1°C. higher than the other. If the deflection on the scale is 150 from zero, then each degree of the scale equals $\frac{1}{150}$° C. When this is ascertained the thermo-elements, or "needles," as they are called, may be used as already indicated, the deflection being proportionate to the difference in temperature between the tissues; or one may be kept in a bath at about the body temperature, in which is a delicate thermometer, so that the temperature may be kept constant. The amount of deflection is then proportionate to the difference between the temperature of the tissues examined and that of the source of constant heat.

The needles are often compound, *i.e.*, consist of several junctions, as thereby the current produced is increased.

In addition to the thermopile, an "electrical resistance" thermometer is sometimes used in the study of slight variations of temperature. It is constructed on the principle that a fine wire undergoes alteration in electrical resistance when its temperature is raised.

The micro-unit of heat is the amount required to raise one milligram of water 1° centigrade, and it has been estimated that the large muscles of the frog give out at one contraction about three micro-units for every gram weight of the muscle, the heat being the result of explosive changes ending in the production of CO_2 and sarcolactic acid. These changes, as already indicated, are not due to immediate but to some precedent oxidation, and may either occur in the muscle substance itself or in some complex body stored up to serve as fuel; and inasmuch as nitrogenous waste is not incurred in contraction, the latter would seem the more probable.

The proportion which the work done by a muscle bears to the heat production varies. Under some circumstances, both the heat and the work done increase together, as when a muscle loaded with increasing weight is stimulated with maximal shocks and made to contract to its fullest extent, the heat maximum being, however, the first attained. We cannot give the exact relation between the sum total of energy producing the contraction and the heat evolved and work done. Generally speaking, the greater the resistance the more work is done in proportion to the heat produced.

Tension has an important relation to the amount of heat produced, which it increases. If the muscle is so fixed that it

cannot shorten, the maximum of heat is obtained, and this is readily seen in the case of dogs or other animals dying from tetanus, in which the temperature may reach 44° or 45°C.

Heat is produced not only during the shortening of a muscle but also during the relaxation, indicating that the latter is a vital action and not merely an elastic recoil; and this is supported by the effect upon relaxation of fatigue and veratria. If a muscle be allowed to contract and loaded just before relaxation begins, more heat is produced than if it had not been loaded.

Under favourable circumstances the proportion of energy which appears as work may rise as high as $\frac{1}{5}$, but it is usually less and may fall as low as $\frac{1}{25}$, the rest being dissipated as heat.

Electrical Properties of Muscle.

Currents of rest; currents of action.—If the gastrocnemius or sartorius muscle of a frog be carefully isolated from the body and a transverse section made through one end, it is found that the longitudinal surface of the muscle is positive to the cut surface, while the latter is negative. Thus, if one electrode be placed upon the uninjured surface and the other on the cut end, a current is sent through the wire, outside the muscle, from the longitudinal (positive) surface to the cut end (negative), and within the muscle *vice versa*, the current passing from the cut end to the uninjured surface; and such a current will deflect the needle of the galvanometer. It is found, moreover, that the equator of

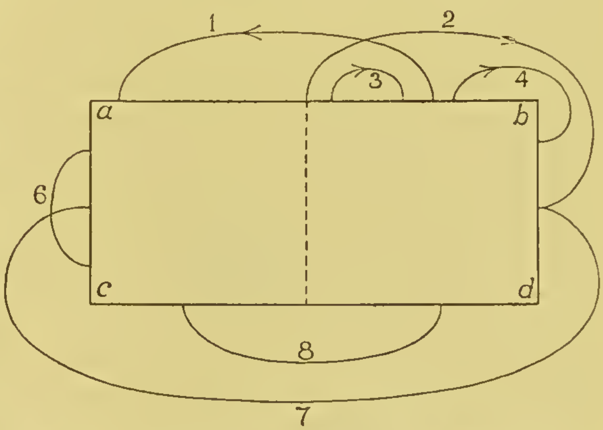


Fig. 124.—Diagram of the Currents in a Muscle Prism.

The arrows indicate currents; their absence the iso-electric condition.

such a muscle includes the points on its longitudinal surface which are most positive, while the centre of the transversely cut end is the most negative point. The further, too, the point chosen on the surface of the muscle is from the equator, the less positive does it become, and the further from the centre

of the cut end the less negative. If two points on the longitudinal surface be chosen equidistant from the equator, they are found to be iso-electrical, and no current is obtained from them. If the points are at different distances from the equator, then the nearer is positive to the more distant, but the current obtained is much feebler than when one of the electrodes is on the cut surface itself. Further, the centre of the cut end is negative to points on the cut surface near to its periphery, and the central point of one cut end of a muscle is iso-electric with the central point of the other cut end.

Du Bois-Reymond supposed that these currents occurred in the normal uninjured muscle, and named them *natural currents* or *currents of rest.* Hermann, on the other hand, contended that a perfectly uninjured muscle is iso-electric in all its parts and that no current was to be obtained from it; and according to his theory, the later one, which is now very generally accepted, Du Bois-Reymond's currents of rest are really *currents of injury*, the injured part becoming electro-negative to the uninjured. And, indeed, it is found that the more care there is taken in isolating a muscle without injury, the less strength there is in the currents to be obtained from it; and doubtless if it could escape injury altogether it would be wholly iso-electric, as the resting heart itself is at all parts of its surface.

The presence of an electrical current in muscle was first observed by Galvani, who noticed that the limbs of some frogs suspended to an iron railing by copper hooks twitched whenever the wind brought them in contact with the metal. The experiment is traditionally demonstrated by isolating the iliac bones and hind limbs of a frog, passing one end of an S-shaped copper hook beneath the sacral plexus, and suspending them to an iron tripod. As the tripod is tilted so that the limbs fall against one of its legs, vigorous contractions take place. Volta considered that the junction of the metals caused the current, the tissues merely acting as a moist conductor, and he constructed the *voltaic pile* on these principles, and from it a continuous current was obtained. But Galvani proved that contraction as the result of a current in the muscle itself was possible. If a nerve-muscle preparation be made, the nerve carefully lifted and allowed to fall along the muscle so that its end comes in contact with the tendinous injured end of the muscle, the circuit of the current of injury is completed and contraction takes place. If the experiment is not at first successful, the injury may be made more pronounced and contraction facilitated by making a clear section just above the tendon, or by injuring the tendinous end with a hot wire.

In Kühne's experiment the current of injury in a nerve stimulates its own muscle to contraction. Two plugs of china clay moistened with normal saline are arranged to project downwards over the edge of a clean glass plate, and the nerve of a nerve-muscle preparation is placed upon them, its cut end in contact with the one, and its longitudinal surface resting on the other. If a watch glass containing normal saline be raised beneath the free ends of the plugs until the fluid touches them, the muscle contracts, owing to the closure of the current of injury in the nerve.

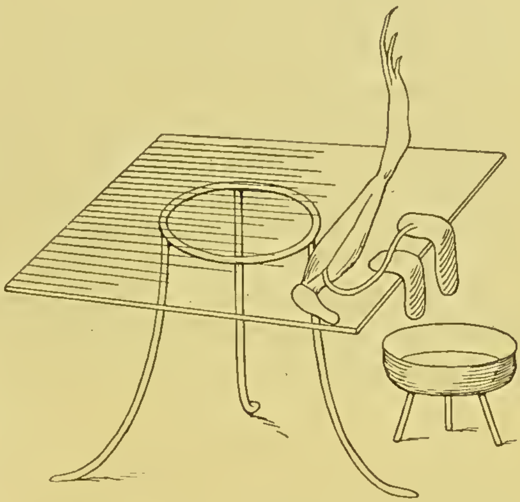


Fig. 125.—Kühne's Experiment.

Again, if two nerve-muscle preparations be taken and the nerve of one, B (Fig. 126), be laid in the form of a loop on the muscle of the other, A, then on tetanising A by means of an interrupted current sent through its nerve, E, *secondary tetanus* is set up in the muscle B. In this case it is the "negative variation" occurring in the muscle A each time a shock is sent in that acts as a stimulus to the muscle B, and produces in it a corresponding tetanus, and of this negative variation we shall now speak more fully.

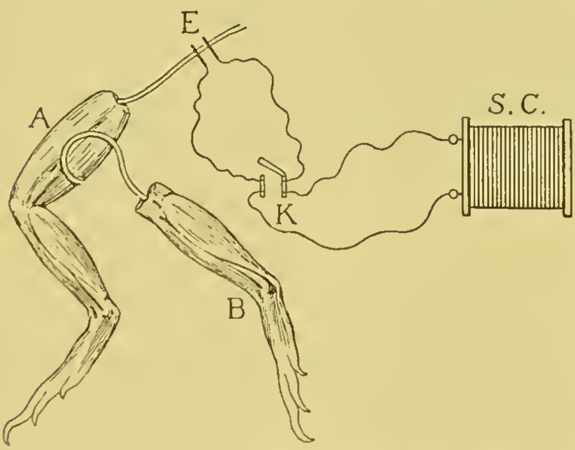


Fig. 126.—Apparatus for Showing Secondary Contraction.

If a nerve-muscle preparation be dissected out carefully, and one non-polarisable electrode be placed upon its tendinous end and

the other over its middle, and the key of the galvanometer be opened so as to allow the current to pass, a slight deflection is usually obtained. If the end be now rendered more negative by injury, the deflection is greater, the spot of light upon the scale travelling further from zero; and this is due to the further development of the "current of injury" by the increased negativity of the end of the muscle. If the muscle through its nerve be now thrown into tetanus, the light swings back towards zero. According to Du Bois-Reymond this was due to a "negative variation" or diminution of the "current of rest" which took place during contraction. The followers of Hermann, on the other hand, consider the diminution in the "current of injury" due to the production of fresh currents from the actively-contracting part of the muscle becoming electro-negative to the portion at rest, and these currents they term "currents of action."

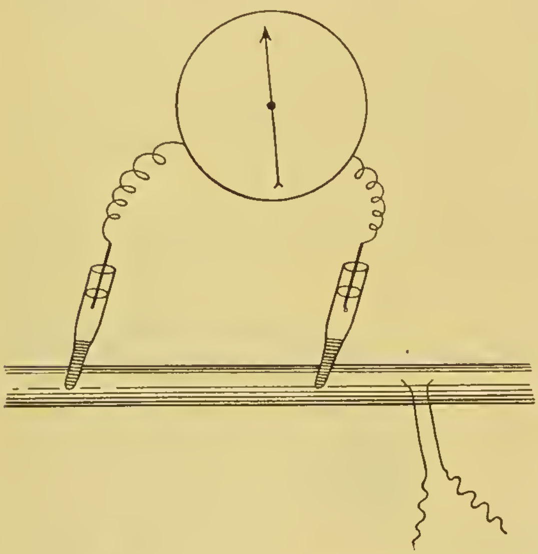


Fig. 127.—Apparatus for Showing Wave of Negativity in Contracting Muscle.

When a muscle contracts, then, it undergoes certain electrical changes, which have been regarded by the followers of Du Bois-Reymond as a negative variation or diminution of the natural current or current of rest, and by those of Hermann, who deny the existence of any but currents of injury, as currents of action; and the latter view seems to have the most evidence in its favour. If any uninjured muscle be taken, and the galvanometer electrodes be placed on two iso-electric points, then when the circuit is completed no deflection of the light takes place. If, now, one end of the muscle be stimulated with a single induction shock, a "wave of negativity" passes along the muscle, a wave which takes place in the latent period alone, and so precedes the physical one. The result of this wave upon the electrical condition of the muscle is that the part through which it is passing becomes negative to the resting part, and thus a current of action from the resting part through the galvanometer to the stimulated part takes place,

and causes a deflection of the light in the corresponding direction. But as soon as the wave has reached the resting part, and left that first affected, a current of action in the opposite direction takes place, as the now active portion of the muscle is negative to that which was previously active and is now at rest, causing a second deflection of the light in the reverse direction to the first; and the electrical change is thus *diphasic*. If a tetanising current be substituted for a single induction shock, the result is the same, but the light remains at zero, and does not show the diphasic character of the electrical change, as the inertia of the magnet is sufficient to prevent it following the individual events which succeed each other with great rapidity, and only the "sum" of these results is shown.

For demonstrating slight changes of electrical potential, the *capillary electrometer* is in common use. In this instrument

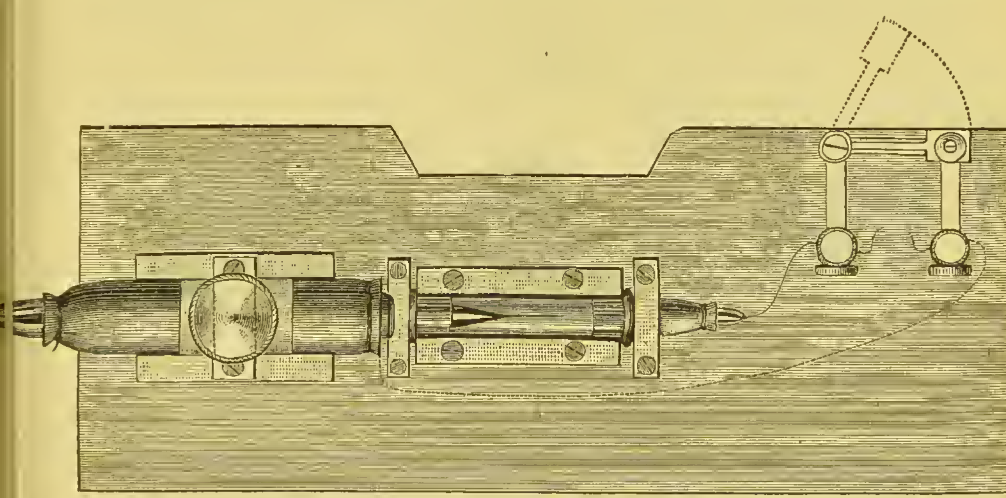


Fig. 128.—Capillary Electrometer.

the surface tension of a thread of mercury in a capillary tube, dipping into a 10–20 per cent. solution of sulphuric acid, is altered, and the mercury travels in the direction of the current causing the alteration. The mercury in the capillary tube is connected with a small pressure bottle containing mercury. The changes in the capillary tube can be watched under the microscope, and may be photographed on a rapidly-moving plate to show the electric change, while the time-tracing and muscle curve may be taken simultaneously.

"The difference in level of the mercury in the pressure apparatus is a measure of the capillarity, and therefore of the difference

of potential. By measuring the pressure when the position of the mercury in the capillary is brought back to its initial position while a current is still passing through it, the instrument may be graduated and can then be directly used as a measurer of small currents." (Brodie).

The negative variation may very readily be demonstrated, however, with the galvanometer if a muscle be used which already shows the current of rest (or injury). If an ordinary nerve-muscle preparation be taken and the tendinous end removed by a clean transverse cut, and the electrodes placed the one upon the equator of the muscle and the other on the cut end, a marked deflection of the light occurs upon the scale of the galvanometer. If the nerve be now stimulated by the interrupted current, the muscle passes into tetanus and the light swings back almost to zero.

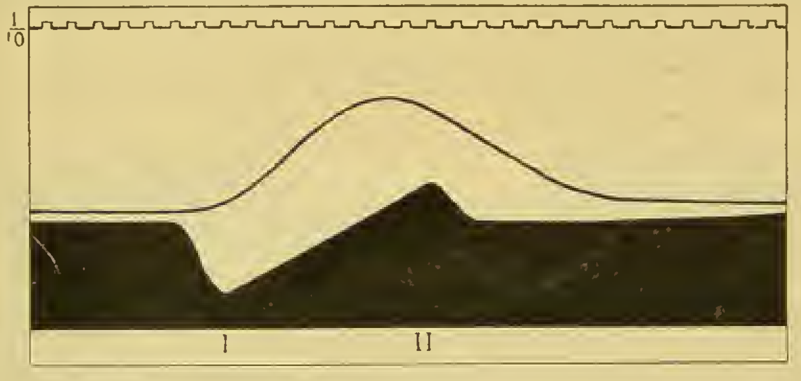


Fig. 129.—Frog's Heart—Diphasic Variation.

Simultaneous photograph of a single beat (upper black line), and the accompanying electrical change indicated by the level of the black area, which shows the varying level of mercury in a capillary electrometer.

In this case then, differing markedly from that of the iso-electric muscle, the "sum" of the phases during tetanic contraction do not balance each other, and the light moves in one definite direction. How is this to be accounted for? The answer is that this muscle is not iso-electric. If a single induction shock be sent through a muscle injured at one spot, the phase of electrical change associated with this part is curtailed as it contracts less, and thus its negativity to the resting part is not increased but remains fairly constant. Hence the diphasic character of the current of action may entirely disappear, and only the effect of the one phase in the direction opposite to the current of injury remain. We may say that the wave of negativity diminishes as the injured part is approached and finally disappears, so that the

second phase is almost absent; and in tetanising the muscle we merely get the sum of the result of repeated single induction shocks causing a series of action currents, in which the second phase of the electric change in each contraction is nearly absent.

Experiments by Burdon Sanderson, however, seem to show that in addition to the rapid and transient alteration in the potential of the contracting muscle referred to, some more permanent reduction of the potential takes place. If the oscillation of the mercury meniscus in the capillary tube be photographed on a rapidly-moving plate, a "spike" is obtained representing the first and second phases of the electrical condition, the second phase being the shorter of the two; but both are succeeded by a "hump" indicating a more slowly developed and more lasting negativity of the contracting part. If the oscillation with an iso-electric muscle be recorded, only the spike is produced, of which the second phase is the same length as the first, as the second phase is not curtailed, nor is a hump shown in the tracing, for here, as the muscle is iso-electric, any general electromotive change affects it equally, so that no difference of potential is recorded after the passage of the excitation wave, though such a difference may exist. When the muscle is injured, however, the injured part, responding less to the stimulus than the active, becomes less negative proportionately, and so the current of injury, rest, or "demarcation," is diminished. (The term "demarcation current"

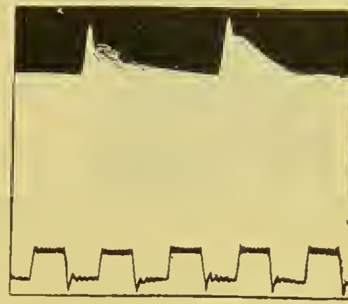


Fig. 130.

Electrical response to single momentary excitations of injured gastrocnemius stimulated indirectly, recorded on a comparatively slowly moving plate, showing a "spike" followed by a "hump." "If the former be taken to mean a sudden electrical swing of such a character as to indicate that the proximal electrode becomes first negative then positive, the latter must indicate that it is followed by a change in the same direction but of slower progress. . . . This slower change not only culminates but begins later, and is therefore called the 'after effect.'" The upper curve is that produced by the movement of the meniscus, the lower is the time tracing. (Burdon Sanderson).

Fig. 131.

The "spike" and "hump" of an injured gastrocnemius muscle, recorded on a plate moving ten times faster than that with which Fig. 130 was obtained. The lowest curve shows the movements of the meniscus, the one above the vibration of the tuning-fork marking time. (Burdon Sanderson).

was employed by the followers of Hermann, because the current, they said, was absent until called into being at the line of demarcation between sound and injured muscle.)

It will be seen from what has already been said that some considerable analogy exists between the effect of a stimulus and an

Fig. 132.—"Spike" of Uninjured Gastrocnemius.

A, Photographed on slow-moving plate; *B*, on fast-moving plate. (Burdon Sanderson).

injury upon a muscle; and it may be that the negativity of the injured surface is due to a continual stream of excitation proceeding from the injured spot itself.

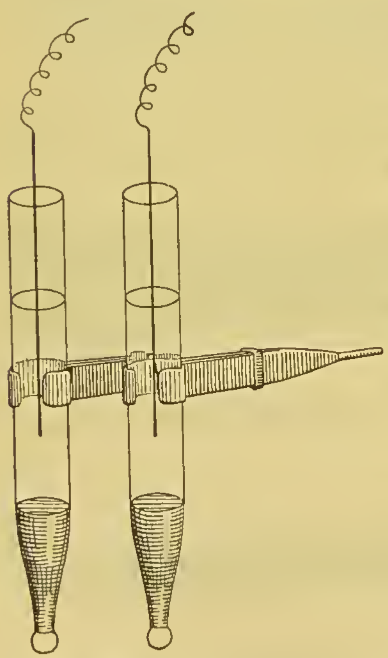


Fig. 133.—Non-Polarisable Electrodes.

Electrical properties of the frog's heart. — The electrometer may be very advantageously used for showing the electrical condition of the heart. If a frog's heart be exposed *in situ*, and one electrode be placed on the apex and the other on the base, no movement of the meniscus of mercury is observed, as the uninjured heart muscle at rest is iso-electric. If, however, the apex be injured, and the electrode replaced in position, a current of injury is set up, and the mercury moves in the direction of it. If the heart be now stimulated to contract, a negative variation of the current occurs, due to a current of action being developed, the second phase of which is curtailed owing to the injury of the apex. If the uninjured beating heart be exposed and

the electrodes placed one on the base and the other on the apex, no current of rest or injury is obtained, but only the diphasic current of action. The contraction, as it sweeps over the heart, renders the base negative to the apex (first phase) and then the apex negative to the base (second phase). Between the two phases a short period may exist during which the heart is iso-electric.

Non-polarisable electrodes.—When ordinary electrodes are used, chemical changes are set up at the point of contact of the wires with the tissues, which lead to the production of currents in the opposite direction, and so are the cause of fallacy in experiments in which small differences are being measured of current or potential. Electrodes in which polarisation does not occur consist generally of a rod of amalgamated zinc dipping into a saturated solution of

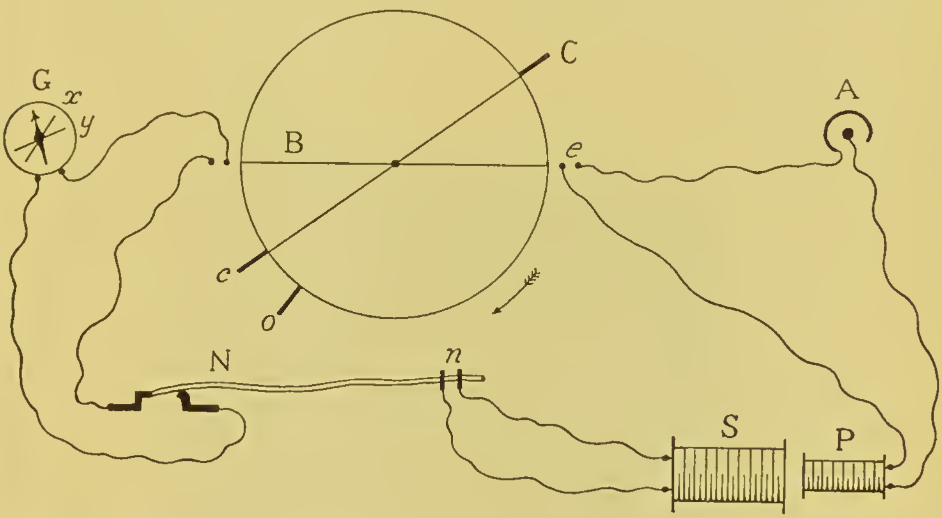


Fig. 134.—Bernstein's Differential Rheotome.

zinc sulphate, the connection with the tissues being made with a plug of china-clay, which fills the end of the glass tube containing the zinc solution and projects slightly beyond it. The clay on the outside of the tube is moistened with normal saline.

The *differential rheotome* of Bernstein enables us to calculate the rate of transmission of the wave of negativity in a muscle or nerve. Fig. 134 shows the arrangement. When the disc B is rotated, C closes the stimulating circuit at *e*, while *c* closes the galvanometer circuit at the same moment. A strong current, the current of rest or injury of the nerve N, causes the galvanometer needle to deflect to *y*. The stimulating current passing into the nerve at *n* has no effect, as it has not time to reach the portion of

the nerve from which the deflecting current was obtained. If, however, the key c be put back to o, the stimulating current has time to traverse the nerve before the galvanometer circuit is made, and there is a marked negative variation of the current of rest, the needle passing back to x. By ascertaining the rate of rotation of the disc, it is easy to calculate the rate of transmission along the nerve.

CHAPTER IV.

THE PHYSIOLOGY OF NERVE.

THE **general structure of nerve fibres and nerve cells.**—The nervous system consists of nerve fibres and cells, supported by connective tissue containing blood-vessels and lymphatics and small nerves, the "nervi nervorum." It may be divided roughly into two main divisions, the *cerebro-spinal* and *sympathetic*, the former including the brain, spinal cord, and the nerves to the

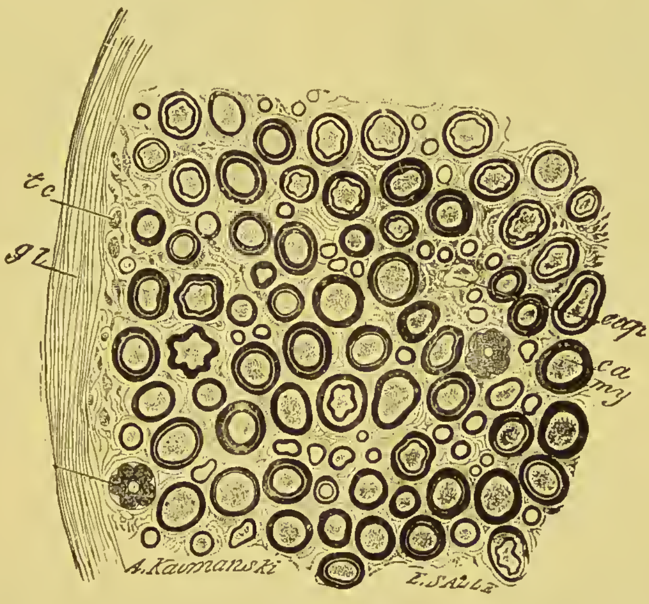


Fig. 135.—Transverse Section of Sciatic Nerve of Dog (×400).

gl, Lamellated sheath (perineurium); *tc*, endoneurium; *my*, medullary sheath of nerve fibre, stained black with osmic acid; *ca*, axis-cylinder; *cap*, blood capillary.

muscles, the latter the chain of ganglia on either side of the spinal column, the plexuses on the viscera, &c. Fibres from the spinal cord pass to the sympathetic ganglia, which in turn give off branches which join the large cerebro-spinal nerves, so that the two systems are in close relation with each other.

The **nerve fibres** are the conducting medium between the nerve cells and the termination of the nerve fibres in the tissues, or between two or more nerve centres, and do not of themselves originate nerve impulses. They are of two kinds, *medullated* and *non-medullated.* A medullated nerve fibre consists of—(1) An axis-cylinder, the functionally active part of the fibre; (2) the medullary sheath; and (3) the neurilemma or grey sheath.

The axis-cylinder is continuous throughout the fibre, extending from the nerve cell (one of whose processes—the *axis-cylinder process*—it is continuous with) to the termination of the fibre, and

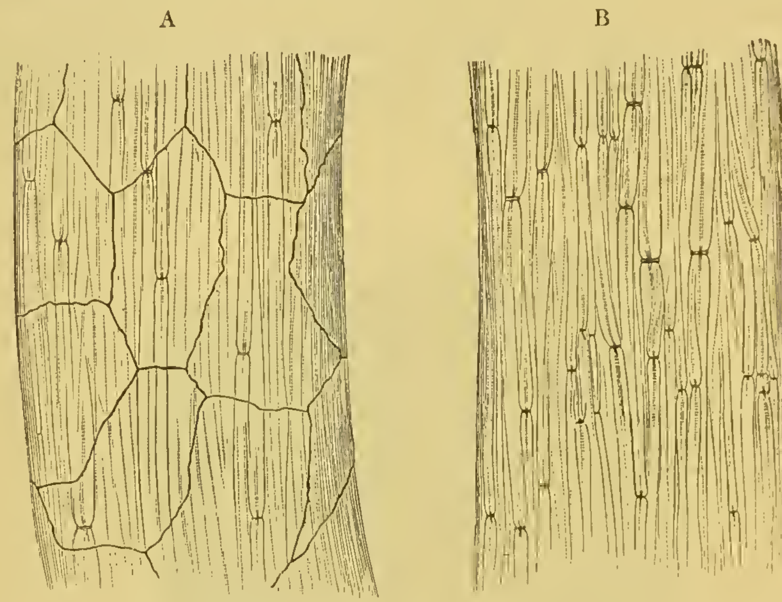


Fig. 136.—Thoracic Nerve of Mouse, Formed of a Single Nerve Bundle, Stained with Nitrate of Silver (×200).

A, The epithelium outlined by the reagent is shown, and through it the crosses of Ranvier may be seen; *B*, the epithelium covering the nerve bundle has been removed, and Ranvier's crosses are more clearly shown.

consists of a transparent, slightly-granular substance which shows fibrillation after death. It is usually about $\frac{1}{3}$ the diameter of the fibre itself, the latter varying from 2 to 20 μ. Outside the axis-cylinder, and presenting a double contour on each side of it, is the medullary sheath, consisting of a fatty substance—myelin—enclosed in a meshwork of neuro-keratin. The myelin may be dissolved out by ether or other solvents, and stains black with osmic acid. The medullary sheath is interrupted at regular intervals along the course of the fibre, these interruptions being termed the "nodes of

Ranvier." If the fresh fibre be subjected to the action of nitrate of silver solution, the reagent permeates it at this point, extending a little way along the axis-cylinder on each side of the node, and the reduction of the salt gives rise to the production of *Ranvier's crosses.* The neurilemma—a thin, transparent membrane—lies immediately upon the medullary sheath, or sheath of Schwann, as it is sometimes called, and at the nodes of Ranvier dips towards the axis-cylinder.

Fig. 137.—Medullated Nerve Fibres from Sciatic Nerve of Frog, Stained with Osmic Acid (×350).

e, Constriction — Ranvier's node; *i*, incisures; *ca*, axis-cylinder; *r*, medullary sheath; *p*, grey sheath.

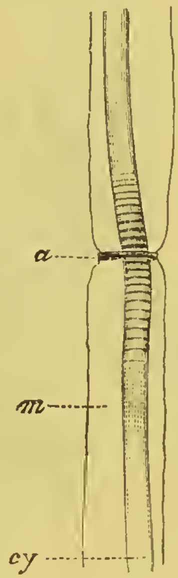


Fig. 138.—Nerve Fibre from Sciatic Nerve of Rabbit, Stained with Nitrate of Silver (×600).

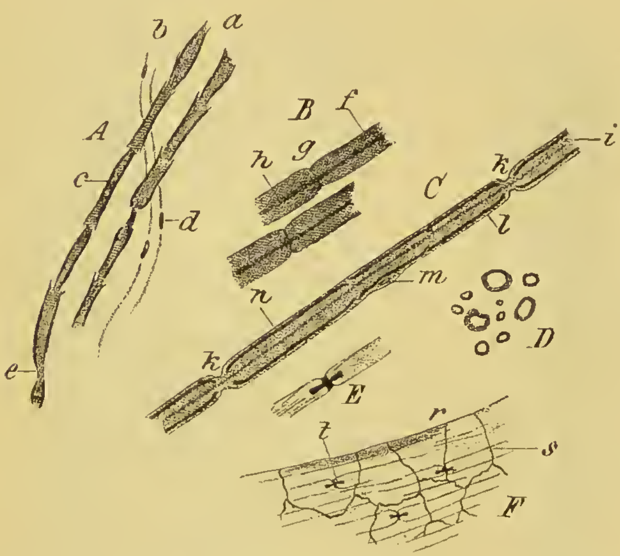
a, Annular constriction—Ranvier's node; *m*, medullary sheath; *cy*, axis-cylinder, showing Frommann's lines, cross striations seen here in the neighbourhood of the node only, but in the isolated axis-cylinder throughout its length.

After death a change takes place in the medullary sheath, by which it becomes split up into cone-shaped imbricating segments, the intervals between them being the incisures of Schmidt and Lantermann. In each internode an oval nucleus is present between the medullary sheath and the neurilemma, embedded in a

little undifferentiated protoplasm—the remains of the protoplasm of the original cell forming the internode. The latter has in development become folded round the axis-cylinder (which is simply a process of a nerve cell) and converted to medullary sheath and neurilemma. The sheaths are probably mainly protective, but it may be that the medullary is also insulating.

The fibres are collected into fasciculi surrounded with connective tissue, and of these several in the larger nerves go to form the nerve trunk. The connective tissue enveloping the whole nerve

Fig. 139.



A. Nerve of Frog, Stained with Osmic Acid (×200).

a, Medullated fibres; *b*, non-medullated fibres; *c*, segments of Schmidt; *d*, nuclei; *e*, node of Ranvier.

B. Longitudinal Section of Mammalian Nerve Fibre at Node of Ranvier (×300).

f, Grey sheath; *g*, node showing transverse line; *h*, axis-cylinder.

C. Semi-Diagrammatic Representation of Medullated Nerve Fibre.

i, Axis-cylinder; *k*, node of Ranvier; *l*, medullary sheath; *m*, nucleus; *n*, grey sheath.

D. Transverse Section of Nerve Fibres (×200).

E. Ranvier's Node, Stained with Nitrate of Silver (×200).

F. Portion of Nerve of Frog, showing Ranvier's Crosses and Outlines of Epithelial Cells (×50).

t, Ranvier's cross; *s*, epithelial outline; *r*, edge of nerve bundle.

is called the *epineurium*; the lamellæ round the fasciculi of nerve fibres, the *perineurium*; and the delicate tissue between the nerve fibres themselves, the *endoneurium*.

In the nerve trunk the fibres do not branch, but they do so on approaching their termination peripherally, and division takes place at a node of Ranvier. As the nerve trunk itself divides and gives off branches, each of these is surrounded by a continuation of the connective tissue sheath of the parent trunk. When the smaller subdivisions are reached, consisting, it may be, of only one or two

fibres, the sheath becomes much diminished and is represented by a few, thin, flattened cells and white fibres. It is then called the sheath of Henle.

Medullated nerve fibres form the greater part of the brain, spinal cord, and cerebro-spinal nerves: those of the brain and spinal cord having no grey sheath or neurilemma. At their termination peripherally, the fibres run between the muscle fibres of the muscle which the nerve supplies, and each muscle cell receives its nerve fibre about its middle. As already stated, the medullated fibre sometimes branches at a node of Ranvier, and so one fibre

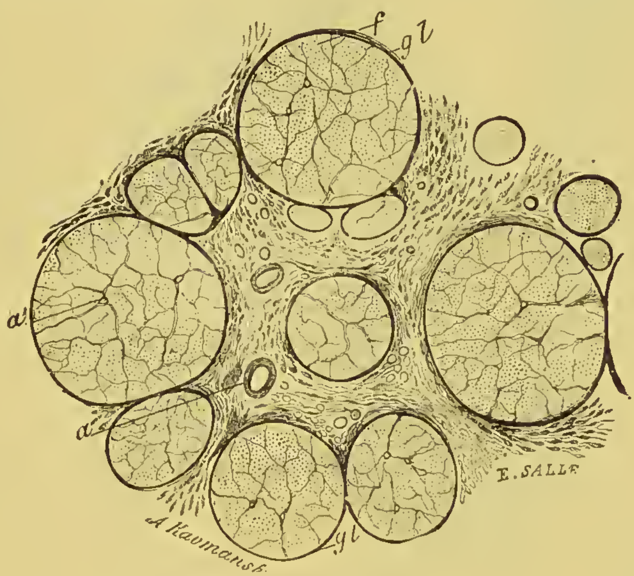


Fig. 140.—Transverse Section of Sciatic Nerve of Man (×20).

gl, Lamellated sheath of nerve bundle ("perineurium"); *a*, artery in connective tissue between the bundles ("epineurium"); *a'*, small artery in the connective tissue between the nerve fibres themselves ("endoneurium"); *f*, nerve fibres.

may supply two or more muscle cells. The nerve plunges into a low, conical eminence at the side of the muscle cell, the neurilemma becoming continuous with the sarcolemma, and the medullary sheath stopping short. The axis-cylinder then divides in a somewhat arborescent manner, the branches anastomosing with each other, the terminal ones being free and club-shaped. Here and there, upon the course of the branches, granular nuclei may be seen. This development of the axis-cylinder rests upon the somewhat oval, flattened *sole* or *bed* of the plate, a granular

material which is, however, distinct from it, and in which may be seen several clear nuclei (page 87).

The motor end-plate may represent the electrical plate of certain fishes, such as the torpedo, malapterurus, &c., the plate having in these developed at the expense of the muscular substance; the whole of the nerve energy in this case being devoted to the production of shock, as opposed to muscular work.

A non-medullated nerve fibre (Fig. 142) resembles the medullated, but has no medullary sheath. Nuclei lie upon its surface at intervals between the axis-cylinder and the grey sheath. The

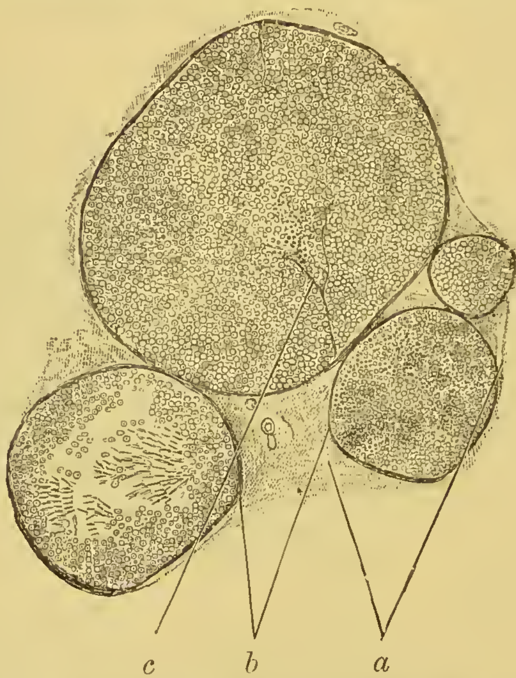


Fig. 141.—Transverse Section of Peripheral Spinal Nerve of Rabbit (×50).

a, Part of epineurium; *b*, perineurium; *c*, endoneurium. In the lower nerve bundle on the left some of the more centrally-placed fibres are seen cut obliquely.

fibres branch and form plexuses and divide into finer filaments at their point of distribution in the walls of blood-vessels, secreting organs, &c. They are found in the grey matter of the spinal cord and brain, the sympathetic ganglia, the nerve plexuses, and intermingled with medullated fibres in the cerebro-spinal nerves.

The **connective tissue** of the nerves and ganglia consists of cells and white fibres, with a small admixture of yellow. The grey and white matter of the brain and spinal cord contains *neuroglia* (see central nervous system) which serves to support the proper nerve

elements. The pia mater also contributes septa of ordinary connective tissue, bearing blood-vessels.

The **nerve cells** differ in histological character in different situations. There

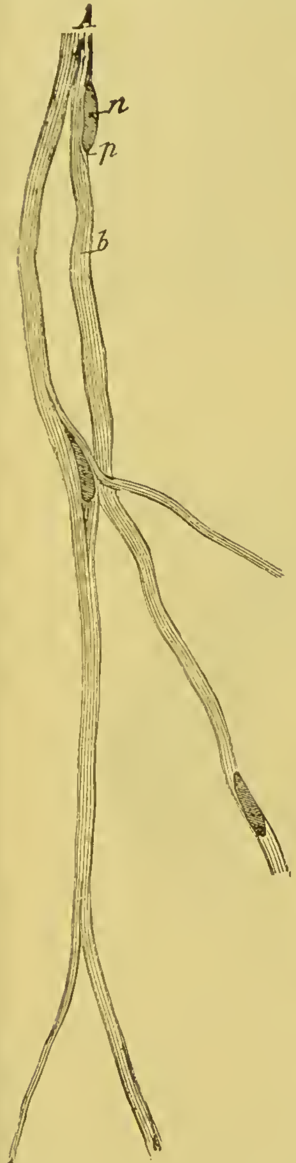


Fig. 142.—Portion of Network of Fibres of Remak from the Pneumogastric of the Dog ($\times$400).

A, Two non-medullated fibres; *n*, nucleus; *p*, grey sheath; *b*, striation due to the fibrils of axis-cylinder.

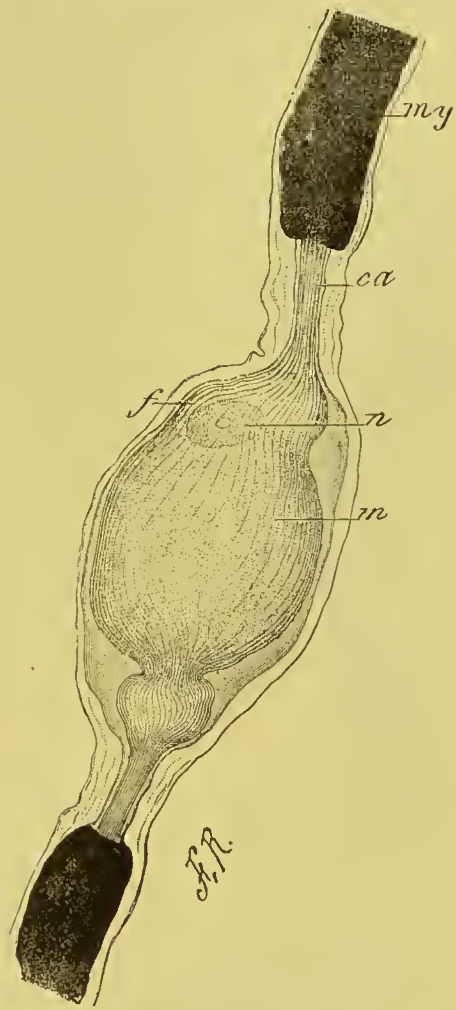


Fig. 143.—Bipolar Nerve Cell from Spinal Ganglion of Skate, Stained with Osmic Acid ($\times$350).

my, Medullary sheath; *ca*, axis-cylinder; *m*, nerve cell; *n*, nucleus; *f*, fibrils from the axis-cylinder, spreading out as they enter the ganglion cell.

are—(1) Unipolar and bipolar cells; (2) multipolar cells of the sympathetic ganglia; (3) multipolar nerve cells of

the spinal cord; (4) pyramidal cells of the cerebral cortex; (5) antler cells of the cerebellar cortex; and (6) granule cells of the cerebellar cortex.

(1) *Bipolar nerve cells* are typical in the spinal ganglia of the skate (Fig. 143). The cell is somewhat rounded, but drawn out to two poles, each of which is connected with an axis-cylinder process. There is a nucleus and well-marked nucleolus, and the grey sheath of the nerve fibres joining the cell is continued over it as a nucleated capsule, the nuclei corresponding to those of the nerve fibres. The splanchnic ganglia of the frog afford another instance of a bipolar cell,

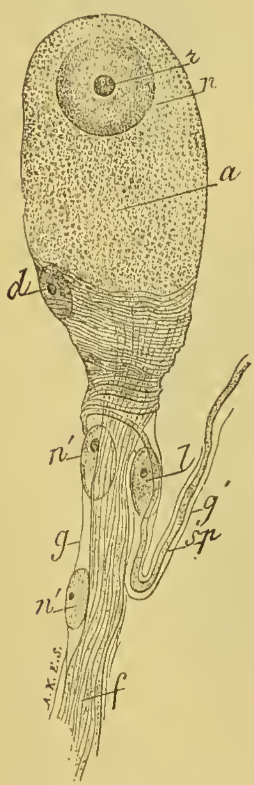


Fig. 144.—Ganglion Cell of Pneumogastric of Frog.

a, Protoplasm of nerve cell; *n*, nucleus; *r*, nucleolus; *d*, nucleus of the capsule; *f*, straight nerve fibre; *sp*, spiral fibre; *g*, *g'*, sheath of Henle; *n'* nucleus of Henle's sheath; *l*, nucleus of Henle's sheath of spiral fibre.

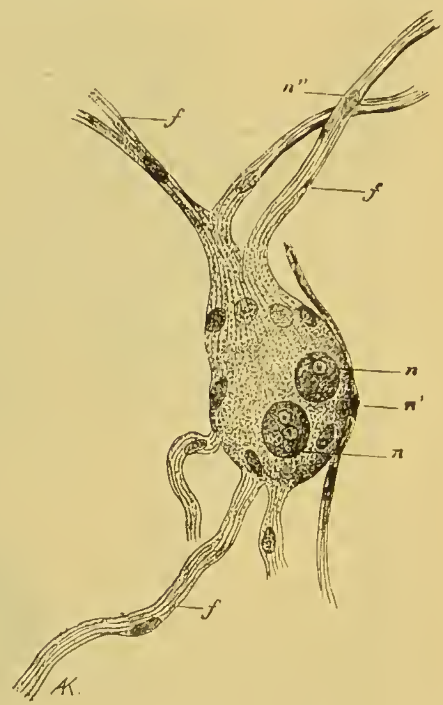


Fig. 145.—Ganglion Cell from Superior Cervical Ganglion of Rabbit.

f, *f*, Fibres of Remak (non-medullated fibres); *n'*, *n''*, nuclei of the fibres; *n*, *n*, nuclei of the ganglion cell.

in which, however, the axis-cylinder processes proceed from the same end apparently, the one coiling round the other, which is straight. Here, again, there is a nucleated capsule to the cell, continuous with the grey sheath. The axis-cylinder processes

pass in opposite directions after leaving the cell, and quickly acquire a medullary sheath. *Unipolar nerve cells* so-called are found in the spinal ganglia of mammals. The two processes of the cell are here fused together as they leave it, but separate at the first node of Ranvier, and pass in opposite directions. Here, again, the cells have a thin nucleated capsule, but outside this is an additional thin lamina of connective tissue which is continued on to the nerve fibres as the sheath of Henle. (2) *Multipolar cells of the sympathetic ganglia* possess only one axis-cylinder process, but several others which do not acquire a medullary sheath. (3) *Multipolar nerve cells of the spinal cord* consist of a mass of delicate protoplasm, containing a large nucleus, with a

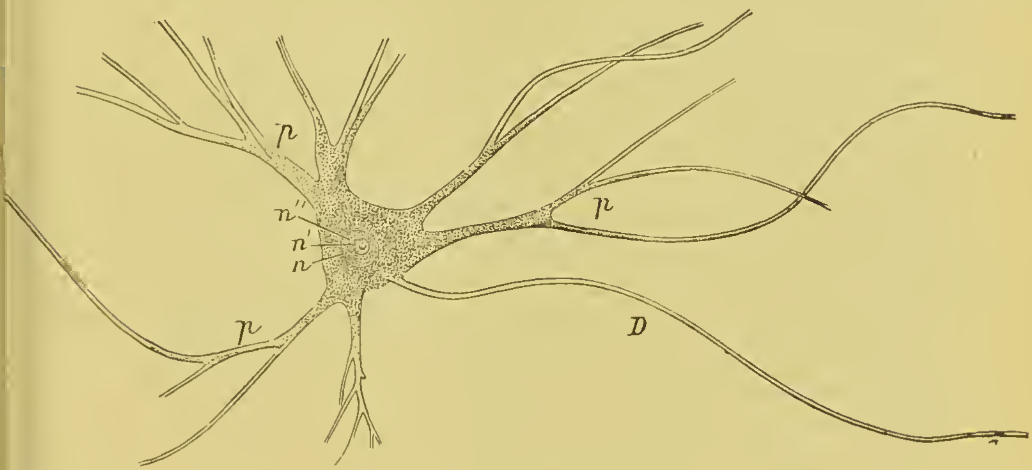


Fig. 146.—Multipolar Nerve Cell from Anterior Horn of Grey Matter of Spinal Cord of Calf (×170).

n, Nucleus; *n'*, nucleolus; *n''*, endonucleolus; *p*, protoplasmic processes; *D*, axis-cylinder process.

well-marked nucleolus. Fibrils enter the protoplasm from the processes of the cell and course through its body. It possesses many processes, one of which becomes continuous with the axis-cylinder of a nerve fibre, and is hence called the *axis-cylinder process* or *neuron*, and this in its turn gives off a few slender collateral filaments. The other processes are called *dendrons*, and these break up at a short distance from the cell into an anastomosing network of fibrils, in which they lose themselves. The neuron or axis-cylinder process (unless it passes out of the cord in the anterior nerve root) ultimately breaks up into a brush of fibrils, which come into physiological if not into mechanical continuity with the dendrons of other nerve cells. (4) The *pyramidal cells of*

the cerebral cortex possess several dendritic processes, and also one axis-cylinder process, which passes off from the base of the cell to terminate in the cord in a brush of fibrils around a nerve cell of the anterior horn of grey matter. Each cell has a nucleus and well-marked nucleolus. (5) The *antler cells of the cerebellum* possess several dendrons (which, by their manner of branching, give rise to the name "antler") and one axis-cylinder process, which breaks up to form a basket-like arrangement of fibrils in which the cells lie; and the basket-work becomes physiologically continuous with the brush in which the neuron from a cell in Clarke's column ends. (6) The *granule cells* of the cerebellum are smaller than the other nerve cells of the brain and spinal cord. They possess an axis-cylinder process and dendrons, and a large nucleus, which stains deeply with hæmatoxylin.

Generally speaking, when the nerve cell in the spinal cord transmits impulses upwards, its axis-cylinder process passes in that direction; and when downwards, it passes downwards. Thus the axis-cylinder processes of the cells in Clarke's column will pass upwards and end in a brush of fibrils round the antler cells of the cerebellum; the axis-cylinder processes of the pyramidal cells of the cerebral cortex will pass downwards and end in a brush of fibrils round the multipolar nerve cells of the anterior horn; and the axis-cylinder processes of these cells may pass further down and terminate again in a brush of fibrils round similar cells at a lower level, and so on; or they may pass directly out in the anterior nerve roots to the muscles.

Development of nerve tissue.—The nervous system is developed from the epiblast, which is invaginated to form the neural canal and tube, the anterior part of which becomes dilated to form the vesicles of the brain, &c., while the posterior forms the spinal cord. The cranial nerves are developed from what is known as the "neural band," consisting of two laminæ connecting the dorsal edge of the neural canal with the external epiblast. The posterior roots of the spinal nerves arise, in a somewhat similar way, from the spinal cord as a nerve rudiment which soon becomes separate (though still applied to the surface of the cord) and shows a proximal rounded portion, an enlarged middle portion, and a distal portion—the commencement of the nerve. The proximal part soon unites with the spinal column again, anterior to its first point of origin. The anterior nerve roots appear to grow from the spinal cord in much the same way, and the combined roots form the whole nerve, which grows constantly outwards with the growth of the embryo.

The sympathetic system is developed in connection with the posterior spinal ganglia. The later development of the system has hitherto been supposed to be intimately connected with that of the suprarenal bodies.

Functions of nerve cells and fibres.—A nerve cell acts as a battery in producing from chemical energy the impulse which is transmitted along the nerve fibre, as electricity is along a wire; but the comparison is not complete, as with the nerve cell and its process no closed circuit is required. The nerve impulse may also be started in the course of the fibres, independently of the cell, by the application of electrical, thermal, mechanical, or chemical stimuli. In the body, however, the impulse starts either in the nerve cell or the termination of the nerve at the periphery, and not in the course of the fibre itself. The change in the nerve as the impulse passes along it is an electrical one, resulting in the production of secretion, muscular contraction, &c., as the case may be; but the cause of the change—whether chemical or due to mechanical vibration—is not determined.

Though, on applying the electrodes to any point of an excised nerve, a wave of nerve impulse passes outwards in both directions, in the body itself the impulses pass along a fibre in one direction only, *i.e.*, from the centre to the periphery, or *vice versa*. We may investigate the normal direction of that impulse and the effect it produces (1) by section of the nerve in its course, and (2) by stimulation of the central and peripheral ends of the cut nerve. Section of such a cerebro-spinal nerve as the sciatic produces immediate loss of sensation and the power of movement in the parts supplied by it; and we then conclude that it contains nerve fibres which carry impulses (motor) down to the muscles, and others which convey sensory impulses from the area of its distribution to the brain. We can verify this conclusion by stimulating the peripheral end of the cut nerve, when we get contraction of the muscles supplied, or the central end, when pain is the result; and similarly with other nerves when their influence on secretion, it may be, and not contraction, is in question.

Changes in nerve fibres after their section.—When such a nerve as the sciatic has been divided, immediate loss of motion and sensation occurs, as already stated; but there are further changes in the nerve trunk itself, which take a longer time to betray themselves. The immediate paralysis is due merely to the severance of the conducting fibres, and denotes no change in the nerve itself. In a short time after section, however, the

excitability of the nerve on either side is raised, the increase radiating from the cut ends; but this soon gives way to diminution, which ends in complete loss in one or two days, the condition extending from the point of section to the peripheral distribution of the nerve. This loss of excitability, proceeding from the centre outwards (centrifugal), is often known as the *Ritter-Valli law*, and is followed by histological changes in the same part of the nerve, *i.e.*, below the point of section. These take place progressively and centrifugally, and occupy about a fortnight in attaining completion. The medullary sheath breaks up into globules of myeloid substance, the axis-cylinder undergoes disorganisation, and multiplication of the nuclei under the grey sheath takes place, leaving in the end a fibrous cord in place of the functionally active nerve; and this degeneration extends down to the terminations themselves, involving even the end-plates in the muscle. At this stage the muscle is itself irritable, but its irritability has undergone a change. It is now more sensitive to the make and break shock of the constant than of the induced current. This condition reaches its height about the seventh week after section, and is succeeded ultimately by total loss of irritability and atrophy.

On the other side of the section, degeneration proceeds along the fibres as far as the next node of Ranvier only in each, and it is from this point that regeneration of the nerve commences, fresh axis-cylinder processes being thrown out, which grow among and between the degenerate ones of the distal end. Sensation is first recovered and then movement more slowly.

What are the causes of this degeneration? Why does it affect the distal portion of the cut nerve and spare the proximal? Why does regeneration take place only from the proximal end? The explanation of these phenomena is found in Waller's experiments upon section of the roots of a spinal nerve. We have seen that if the nerve be divided below the point of junction of its roots, degeneration takes place in all the fibres of the nerve downwards to the periphery. If the anterior root only be divided, the peripheral end and the fibres forming its continuation in the common nerve degenerate. If the posterior root be divided between the ganglion and the spinal cord, only the central stump and the fibres passing up the cord from it to the medulla oblongata degenerate. Thirdly, if the posterior root be cut between the ganglion and the common nerve, the peripheral end and its fibres in the nerve degenerate. These degenerations result from the fact that the motor nerve cells in the anterior horns of grey matter in the spinal cord are the nutritive centres for the anterior nerve roots, and hence when these are cut, the peripheral portion, being separated

from its nutritive centre, degenerates, and that the ganglion of the posterior root is the nutritive centre for the fibres passing through it, so that when the root is cut on either side, the separated portion of nerve tissue degenerates. In the case of the upper portion the degeneration continues along the fibres till they reach the medulla, when it stops, as here the fibres come into physiological continuity with other nerve cells, which act as nutritive centres to the fibres beyond them.

The motor fibres in the spinal cord have their nutritive centres in the motor areas of the cerebral cortex.

It should be mentioned that on section of the anterior nerve root, certain fibres, though few in number, in the central stump undergo degeneration, and others in the peripheral stump do not.

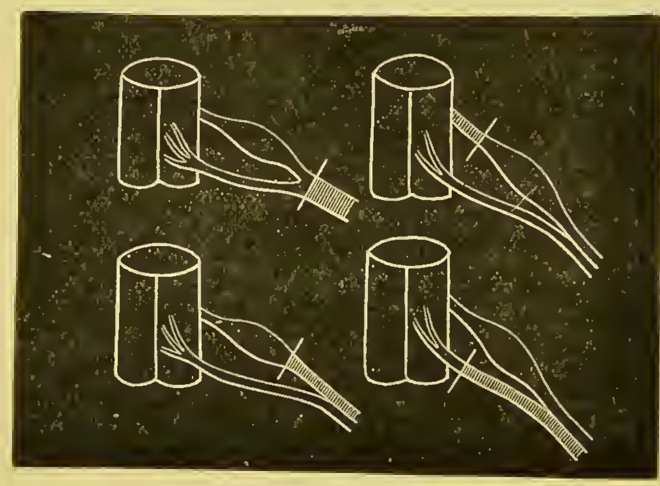


Fig. 147.—Degeneration of Spinal Nerve and its Roots after Section. ("Wallerian Degeneration.")

Degenerated parts shaded.

These are not motor fibres: they are "recurrent" from the ganglion to the pia mater, &c., and hence the part separated from the posterior root dies, while that still connected with it survives.

This nutritive influence of nerve cells upon the fibres with which they are connected has been called a "trophic" one, and the question has been much mooted as to whether the nerve cells have a similar general influence upon the tissues. After section of the trigeminus nerve, ulceration of the cornea, of the lips, &c., frequently takes place, and this has been quoted in favour of the view that they have such an influence. But it is found that with care such ulceration may be greatly postponed, if not prevented;

and the loss of sensibility alone after section, inasmuch as it renders the parts liable to constant irritation and injury, is sufficient to account for the ulceration. There does not seem yet to be any definite proof of trophic action, though in many cases appearances are in favour of it, as in the case of bedsores in people with lowered vitality. But here again other influences come in, as in such people fairly constant pressure, caused by the adoption of one position, may act, it will easily be understood, as a positive injury. It is well perhaps to bear in mind that even if such trophic force were really exercised constantly upon the tissues, it would not be very capable of demonstration, and we may take the very pronounced result upon muscle of separation from the spinal cord by section of its nerve, as contrasted with the effect of mere loss of use of the muscle from some other cause, as an indication that, until further evidence is forthcoming, it may not be wise to exclude decisively the theory of "trophic nerves."

Classification of Nerve Fibres.

1. Efferent fibres.—In these, the impulse passes from the centre to the periphery, and they are therefore sometimes called "centrifugal." An ordinary **motor** nerve fibre passing to muscle is an instance of one of these. An impulse may be generated in such a fibre in many ways. Thus it may be *automatic*, as in the case of the respiratory movement, in which consciousness is not concerned, and the energy is evolved periodically from cells in the medulla oblongata. Again, the impulse may be the result of volition, as when it has its origin in the nerve cells of the cortex cerebri. Thirdly, it may be *reflex*, or *sensori-motor*, the impulse in this case starting from some surface connected with an afferent fibre which stimulates to activity a nerve cell in the spinal cord. Another form of efferent fibre is the **secretory**, and this is found in the chorda tympani nerve supplying the submaxillary and sublingual glands. If this be cut and the peripheral end stimulated, an impulse is transmitted to the glands, causing the secretion of saliva. A third kind of efferent fibre, the **inhibitory**, is found in the vagus nerve to the heart: on stimulation of the peripheral cut end, the heart is slowed or stopped; similarly, the chorda tympani contains inhibitory efferent fibres, for on stimulation of its peripheral cut end, the blood-vessels of the glands dilate.

2. Afferent fibres.—Of these, in which the impulse passes from the periphery to the centre—hence "centripetal"—the commonest instance is the ordinary **sensory** nerve. Here, *e.g.*, in

the skin, we have the nerve arising in the form of fine fibrils among the epithelial cells of the stratum Malpighii, uniting to form a nerve fibre in the connective tissue beneath, and passing in the general nerve to the spinal cord, when it comes into physiological continuity with fibres passing to the sensorium in the cerebrum, where alone sensation results. The special senses require a more complicated mechanism, the receiving plate, as in the eye or ear, being an elaborate structure, which transmits the impulse along the nerve belonging to it to the sensory cells in the brain. Then there are the afferent fibres concerned in any reflex act, whether it be motor or secretory. A reflex act requires for its performance (*a*) an afferent nerve to receive the stimulus and transmit it to (*b*) a nerve cell which becomes energised, and (*c*) an efferent fibre to conduct the fresh impulse outwards to (*d*) the organ acted upon, which may be either muscular or glandular. The nerve cell with its afferent and efferent fibres constitutes the reflex arc. The afferent fibres in these cases are termed, according to circumstances, **excito-motor** or **excito-secretory.** Thus a decapitated frog if uninterfered with will lie quiescent, but if the skin of its back be touched with a solution of sulphuric acid, a movement of the muscles of one or both legs may be produced, the extent of the movements depending on the strength of the stimulus. The spinal cord and medulla are the great centres for reflex actions, which may exhibit very different degrees of complexity, ranging in this case from the simple twitch of a muscle up to complex and co-ordinated movements of a whole limb. In a purely reflex act there is no sensation. If, however, the stimulus be sufficiently great the excitement may spread beyond the reflex arc itself up to the sensorium in the brain, and in such a case the act is called a *sensori-motor* one. Coughing, a complex act, being a violent expiratory effort following irritation of the sensory nerve to the larynx, is sometimes purely reflex, and sometimes sensori-motor. Reading aloud is a distinctly sensori-motor act, while the action of light falling on the retina upon the pupil is as distinctly purely reflex in its nature.

The nerve of taste is an instance of an excito-secretory nerve, the impulse passing from the mucous membrane of the mouth to the centre for salivary secretion in the medulla, which transmits it in turn to the salivary glands. Another class of afferent fibres are the **inhibitory.** The great auricular nerve of the rabbit contains fibres which, when the central cut end is stimulated, cause inhibition of the nerve cells in the medulla presiding over the blood-vessels of the ear, thus causing them to dilate. The depressor nerve of the heart, when its central end is stimulated, transmits impulses to the medulla, inhibiting the action of the nerve

cells presiding over the blood-vessels of the splanchnic area. In addition to the afferent and efferent inhibitory fibres which have been referred to, and which transmit involuntary impulses, there are fibres which convey voluntary inhibition. Thus the will acting from the volitional part of the cortex cerebri can inhibit the action of the respiratory centre for a certain time; and trains of thought can often be inhibited at will.

3. Intercentral, commissural, or associated fibres.—These connect the nerve centres or the cells in them one with another, and are used to transmit impulses when any co-ordinated or complex movements take place. The great majority of the fibres in the brain are commissural.

The special functions of **nerve cells** are to originate the impulses which pass along motor, secretory, and inhibitory nerve fibres; to produce consciousness with all the mental processes of memory, reason, &c.; and to maintain the nutrition of nerves and, it may be, through them, that of the tissues.

The Electrical Properties of Nerve.

Currents of rest and action.—When an impulse is transmitted along a nerve an electrical change takes place, due to some molecular alteration, the nature of which, whether mechanical or chemical, has not yet been determined. The amount of heat generated either by chemical change or mechanical friction is too small to affect the most delicate thermopile, and the electrical change is all we can study in the nerve fibre itself. Though less marked it is the same as that in muscle. If the electrodes connected with a capillary electrometer be placed far apart upon the *uninjured* sciatic nerve, no movement of the meniscus of mercury is observed as the nerve is iso-electric. If an induction shock now be sent in to one end of the nerve A, this end, while excited, becomes negative to the rest, and the electrometer shows a current in the direction C to B (outside the nerve)—the first phase of the change. When the excited state has passed on to C and left B, the former becomes negative to the latter, and a current in the

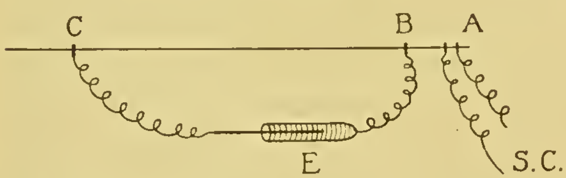


Fig. 148.—Diagram of Experiment Illustrating Currents in Nerve.

opposite direction, from B to C in the electrometer circuit, is the result—the second phase of the diphasic phenomenon.

If the nerve be cleanly cut across towards one end, and one electrode from the galvanometer (in place of the capillary electrometer) be placed against the cut surface and the other on the equator of the longitudinal surface, upon opening the galvanometer key the light is deflected from zero: the cut end being *injured* is electro-negative to the longitudinal surface, as in muscle, giving rise to the "current of rest" (or "injury") of nerve. If faradic shocks are now sent into the other end of the nerve, a "current of action" or "negative variation" causes a reduction in the deflection, as in the case of muscle, because the potential of the uninjured part of the nerve is lowered by the excitation, though it still remains positive to the cut end.

The current of action in a nerve may also be shown by the rheoscopic frog. If the nerve of a nerve-muscle preparation be laid over the equator and cut end of a piece of fresh nerve, and the other end of the latter be stimulated with a single induction shock, the muscle will give a single twitch; with a tetanising current, the tetanic contraction; and, as in the case of muscle already considered, the shock is caused by the negative variation or current of action in the isolated piece of nerve.

If a nerve be stimulated about its middle, the current of action is propagated with equal readiness in both directions, whether it be a sensory or motor nerve.

The **effect of the constant current on the electrical properties of nerve.**—The passage of a voltaic or constant current through a nerve has a marked effect upon the current of rest. If the constant current be sent through the nerve so that its direction be the same as that of the current of rest, the effects of the two are added together arithmetically, whereas if the directions be different, they are added together algebraically. Let a length of nerve be taken, as in the subjoined figure, and the electrodes of a galvanometer be placed at each end so that the current of rest may be shown by the deflection of the needles G and H; and the battery P be arranged so that at closure of the key K, the polarising current will flow through the nerve from p to p^1. On closure of the key a nerve impulse is sent along the nerve in both directions, outside the polarising electrodes, and the needles G and H will give evidence of an instantaneous negative variation or current of action, by a short return towards zero on the part of the spot of light on the galvanometer scale. But with this transient negative variation we have nothing to do, as we are now only concerned with the

condition of *physical electrotonus* of the nerve during the continued passage of the constant current. Here the polarising current is flowing from p to p^1 along the nerve, and thus in the same direction as the current of rest on the left, and in the opposite direction to that on the right. Consequently, the deflection of the needle G is increased, while that of H is diminished, or even turned in the opposite direction if the polarising current be more powerful than that of rest. This condition of physical electrotonus no doubt underlies physiological electrotonus, which will shortly be considered.

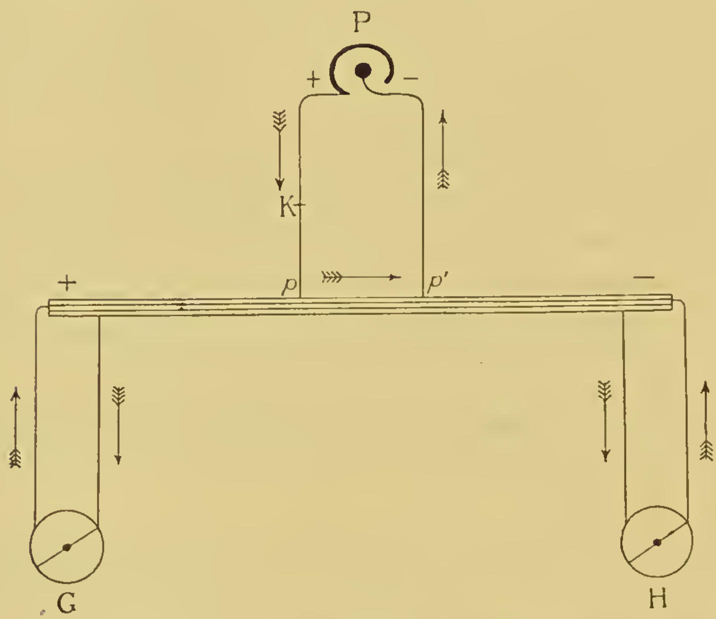


Fig. 149.—Diagram of Experiment Illustrating Effect of the Constant Current upon the Electric Properties of a Nerve.

The **establishment of a nerve impulse by direct stimulation of nerve.**—The effect produced varies (1) with the strength and duration of the stimulus, and (2) with the excitability of the tissue. As an example of the first, if a pithed frog be taken and its toes dipped into very dilute sulphuric acid (1 in 800), and the time be counted in seconds, some little time will elapse before the reflex act of withdrawing the toes from the solution takes place. If the foot be now washed and the toes gently lowered into a much stronger solution (1 in 20), the latent period is much diminished. The weak solution in the first experiment accomplishes the same result as the stronger solution in the second, through the greater length of time the stimulus is being applied,

thus giving the law of the "summation of stimuli" time to be operative. A constant series of impulses passes from the skin surface to the nerve cells in the spinal cord, but no discharge takes place from these till the impulses from the skin, following each other in rapid succession, have attained a certain collective strength. Thus, in such a case, the length of time of application and the strength of the stimulus applied vary inversely to produce the same effect.

The degree of excitability of the nerve is affected by the nearness of the part stimulated to the nerve centre, and by several other conditions. If the sciatic nerve of a frog be divided high up near the spinal cord and exposed to low down in the leg, and stimulated first at the lower cut end, and secondly near the periphery, a greater resulting contraction is obtained as the result of the first stimulation. According to Pflüger's "avalanche" theory, the reason for this was to be found in the nerve wave gathering force the greater the distance over which it travelled. But this seems to be not so, for if the experiment be repeated upon a frog in which the nerve is not divided, and the reflex effect on the opposite side be observed, it is still the part nearest the nerve centre which is most excitable, and leads to greater contraction, though the length of nerve traversed is obviously less (Rutherford). But it is to be noted that in this experiment *a greater number* of afferent fibres are stimulated when the electrodes are applied near to the spinal cord than when they are applied much lower down, and presumably the reflex act involves thereby a greater number of nerve cells in the cord, and so the reflex effect on the other side is naturally greater. It may be that in the first experiment the increased excitability in the upper part of the nerve, *i.e.*, at the seat of section, was due to the commencement of the changes known as the Ritter-Valli law.

Other conditions affecting the degree of excitability are—(1) The nutrition—when this is reduced below normal, the excitability first increases and then diminishes; (2) the temperature—moderate heat raises it and cold lowers it (a wire that has been exposed to extremes of heat and cold will of course act as a stimulus); (3) chemical agents such as ether and chloroform suspend the excitability. The effects of chemical agents may be studied by—(*a*) Faradising the nerve of a nerve-muscle preparation, and observing the resulting contraction, the nerve being in a chamber where it can be exposed to the action of gases, &c.; (*b*) Waller's method of faradising a nerve connected with galvanometer, in moist chamber, and photographing the result of successive negative variations on a slowly-moving plate.

Effect of the constant current on the excitability of a nerve.—When a constant current is sent through a nerve, contraction (of the muscle) generally takes place at the make (closure of the circuit) and at the break (opening of the circuit), but as a rule none takes place while the current is flowing. But though there is no contraction, the condition of the nerve as regards its excitability is markedly changed, and to this condition has been given the name *electrotonus.* The excitability of the nerve is reduced in the region of the positive pole and raised in that of the negative, and hence the area of increased excitability is said to be *kathelectrotonic*, that of diminished excitability *anelectrotonic.* The sudden passage of a portion of nerve from a lower to a higher state of excitability acts as a stimulus, and we can now see why at the make stimulation takes place at the negative, and at the break at the positive pole. When the circuit is closed the part of the nerve presided over by the kathode has its excitability raised, and this acts as a stimulus and contraction follows; but the lowering of excitability in the anodal region, which takes place at the same time, does not lead to stimulation. Upon breaking the circuit the current disappears, and both portions of the nerve return to the normal; and now stimulation takes place at the anode, because of the change in this region from a lowered to a normal, *i.e.*, higher, excitability, but none at the kathode where the excitability is falling down to normal. Thus both at make and break the stimulus is due to the change from a lower to a higher state of irritability. The make shock is the stronger of the two, as the *establishment of kathelectrotonus* takes place more rapidly than the disappearance or *resolution of anelectrotonus*, and the more rapid the change the more effective is the stimulus.

In the case of the make and break induction shock we have seen that the induced current disappears more slowly than it is established, and we probably have to deal with the kathelectrotonic element only as a stimulus in each case, *i.e.*, at both the make and break, the resolution of anelectrotonus being insufficient to start a separate nerve impulse.

The following experiment will illustrate the effect of a constant current on the excitability of nerve. In a nerve-muscle preparation, let the polarising electrodes from a battery, B, be laid upon the nerve at K and A, a commutator, C, being arranged to send the current in either direction, and the stimulating electrodes from an induction coil placed at X between the muscle M and the polarising current. Before throwing in the constant current, close the primary circuit of the stimulating battery, sending in a shock at X, and record the contraction obtained. Now fix the commutator

so that A is the positive electrode and K the negative of the polarising current, and close the circuit. Take a second record of contraction on stimulating the nerve, as before, with a closing shock at X. It will now be found to be greater, because the

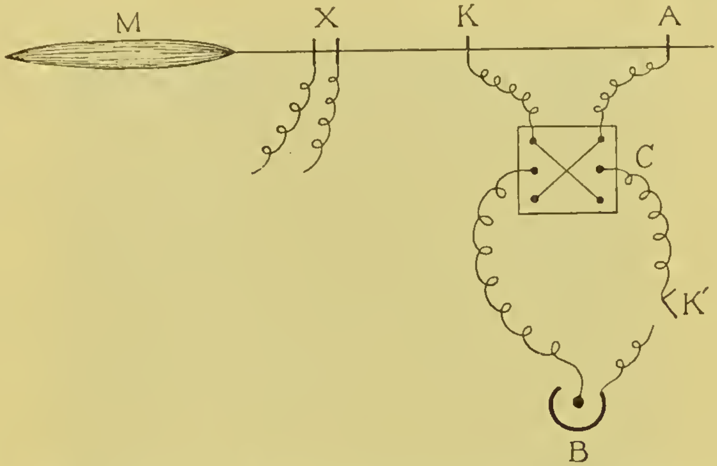


Fig. 150.—Diagram of Experiment Showing the Effect of a Constant Current on the Excitability of a Nerve.

nerve on either side of the kathode K has had its excitability raised (kathelectrotonus), and consequently the same stimulus produces a greater result. If the commutator is now arranged so that K becomes the positive pole and A the negative, and the

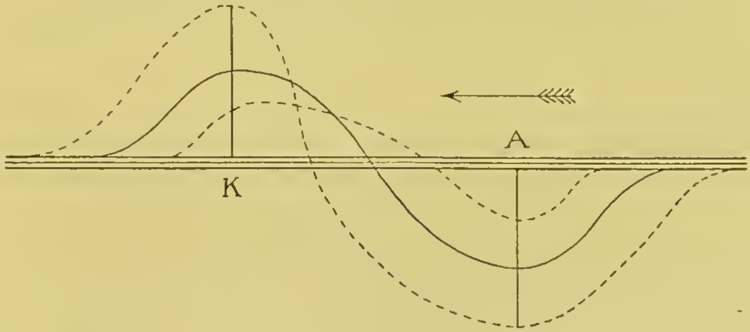


Fig. 151.—Diagram Illustrating the Variations of Irritability during Electrotonus.

nerve be again stimulated at X, it will be found that the contraction is less, as the area presided over by the now positive pole K has its excitability lowered (anelectrotonus).

For convenience, when the kathode is next to the muscle the current is said to be "descending," and when the anode is nearest the current is "ascending."

That the nerve is affected at all at X by the polarising current is due to the fact that the influence of the current extends beyond the poles themselves, affecting as well the whole of the intra-polar region, except at one point—the point of indifference. The intra-polar region is divided between the two influences of excitement and depression, according to the strength of the current. Thus with a weak current, the greater part of it is in a condition of kathelectrotonus, but as the strength of the current is increased, more and more becomes anelectrotonic, the point of indifference gradually leaving the anode to approach the kathode. In the above experiment, instead of the induction current, other forms of stimulation may be employed. A drop of common salt solution on the nerve will produce tetanus, which is increased if the kathode be next to it, and decreased if the position of the poles be reversed; or a tetanising current may be substituted for the common salt.

But not only is the excitability of the nerve influenced by the constant current; its conductivity is also affected. With a moderately strong current the conductivity, *i.e.*, the readiness with which the nerve will transmit an impulse, is markedly *lowered* in the kathodal area, though the anodal is not much affected; if the current be much stronger the conductivity becomes also reduced in the anodal area, though to a less extent. But when the current ceases, *i.e.*, on opening, the conductivity in the anodal area is reduced, while that of the kathodal is restored to the normal. Thus, the raising of the excitability leads to a decrease of conductivity; the lowering of it again to normal to the disappearance of the decrease.

When the make and break shocks of a constant current are used as stimuli, it is found that the reduction of the conductivity has a very important effect on the result obtained, which depends largely on the strength of the stimulus and the relation of the poles to the terminal organ. If a *strong current* be used, C(2), and the current be an ascending one, on make there is no contraction, as the whole of the intra-polar part of the nerve has its conductivity so lowered that it acts as a block; but at break there is contraction as the anode is next to the muscle and there is nothing to stop the course of the excitement started at this point. But if the current were descending and the position of the anode and kathode reversed, on making there is contraction, as the kathodal region is next to the muscle and there is therefore nothing to stop the excitation started here from reaching it. There is, however,

no break contraction, as the anodal area has a reduced eonductivity on opening, and the kathodal area has not yet beeome passable as the current was a strong one. If the eurrent is of *medium* strength, C(1), a eontraction is obtained whether the anode or the kathode be nearer the muscle. If the former (ascending current),

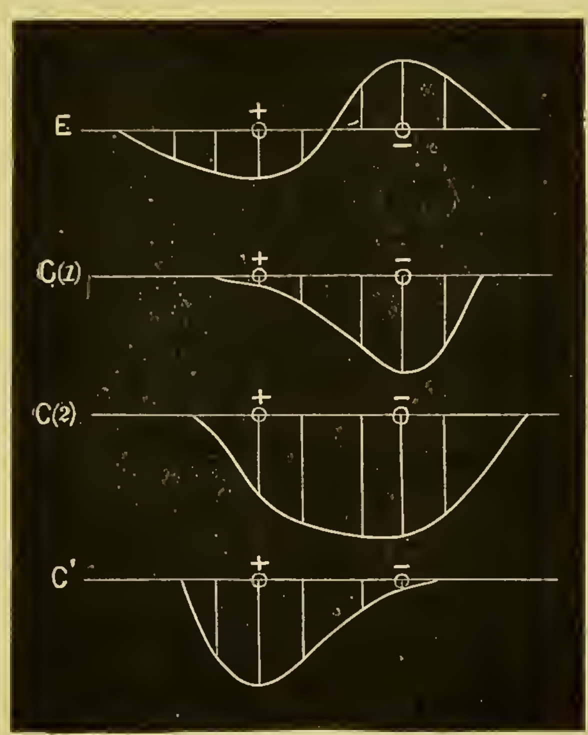


Fig. 152.—Diagram of Changes of Excitability and Conductivity Produced in a Nerve by a Voltaic Current.

E, Changes of excitability during flow of current, according to Pflüger; *C*(1), changes of conductivity during passage of moderately strong current—conductivity greatly reduced round cathode, little affected at anode; *C*(2) during passage of very strong current—conductivity reduced both in anodic and cathodic regions, but less in former; *C′*, changes just after opening a moderately strong current—conductivity greatly reduced in region which was formerly anodic, little affected in region formerly kathodic.

then on making there is nothing to bloek the kathodal stimulus, and on breaking nothing between the anode and the muscle to act as a block. If the kathode be next to the musele (deseending eurrent), then on making the eurrent obviously nothing can eome in the way of a bloek between it and the muscle, and on breaking,

the excitation at the anode readily passes through the kathodal area, the conductivity of which has been restored by the break. With a *weak current*, contraction only occurs at make, whether the direction be ascending or descending, the make being the stronger stimulus, and the break here being subminimal. The conductivity of the nerve is not appreciably affected by weak currents.

The above results have been formulated as Pflüger's law of contraction, and may be thus tabulated:—

CURRENT.	ASCENDING.		DESCENDING.	
	M.	B.	M.	B.
Weak	C	—	C	—
Medium	C	C	C	C
Strong	—	C	C	—

"Law of sensation" would apply to nerves in which the result is sensory and not motor.

That the conductivity of the nerve is lowered by the passage of a continuous current may be readily shown by the following experiment, in which the polarising electrodes are placed upon the nerve, between the muscle and the stimulating electrodes. Let the polarising current be at first short-circuited, and throw in the stimulating shock. If the current be fairly strong, contraction of the muscle takes place, both at the make and break. Now open the short-circuiting key of the polarising current, and again stimulate the nerve as before with an induction shock. There is now no contraction, either at the make or break, the polarising current having so reduced the conductivity of the part of the nerve it passes through that it acts as a block. The same experiment may be varied by using a drop of salt solution, or the interrupted current, to produce tetanus, which disappears as soon as the polarising current is thrown in.

The **velocity of the nerve impulse.**—The rate of transmission of the excited state along a nerve may be measured by stimulating it at two points well apart, and calculating the value of the difference between the latent periods of the two resulting muscular contractions, a record of which is taken upon the plate of the pendulum myograph. Given the length of nerve between the points of stimulation and the difference in the length of the latent

period in parts of a second, the calculation is simple. A nerve-muscle preparation is taken and arranged so that a lever may record the contraction of the muscle on the pendulum plate. The nerve, which should be as long as possible, is supported on two pairs of electrodes connected with a commutator, which in its turn is connected with the secondary coil of the induction machine.

The electrodes should be placed one pair at the proximal end of the nerve and the other near to the muscle. The primary circuit of the induction machine is broken by the falling over of the key of the myograph as the pendulum bearing the plate makes

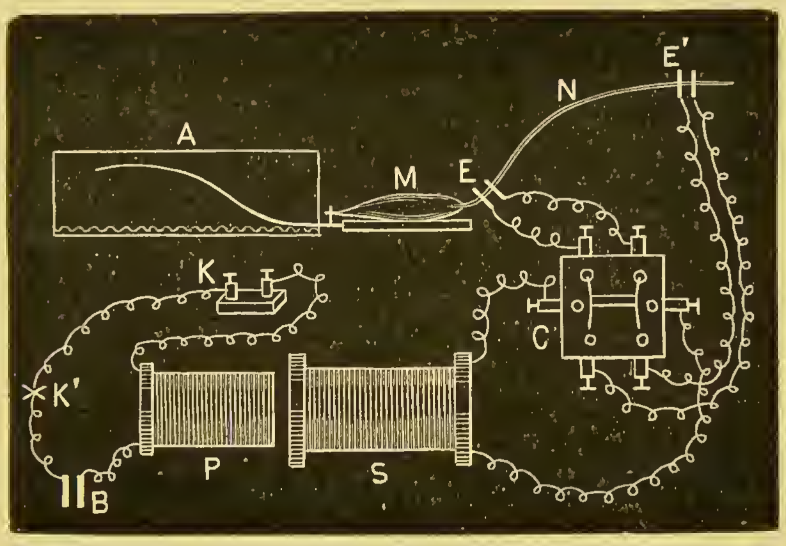


Fig. 153.—Apparatus for Measuring Velocity of Nerve Impulse.

A, Spring myograph plate; *M*, muscle; *N*, nerve; *E* and *E'*, two pairs of electrodes; *C*, Pohl's commutator; *K*, knock-over key of spring myograph; *K'*, opening and closing key of primary circuit; *B*, battery; *P*, primary coil; *S*, secondary coil.

its excursion. The commutator is first arranged so that the nerve will be stimulated next to the muscle, and a tracing is taken in the usual way, with a time record of $\frac{1}{100}$ths of a second beneath it. The apparatus is then arranged as before, but the commutator turned so as to send the shock into the nerve at the other end, and a second tracing taken. The difference between the two latent periods, the latter of which is the longer, gives the time, in $\frac{1}{100}$ths of a second, which the impulse took to travel the length of nerve between the pairs of electrodes, which is measured in millimetres. Thus, if the time were $\frac{1}{300}$th of a

second and the distance travelled 75 mm., the rate per second will be 75 × 300 = 22,500 mm. per second.

In human nerve the velocity is about 111 feet per second; in the frog 80 to 90 feet; but the difference decreases as the same

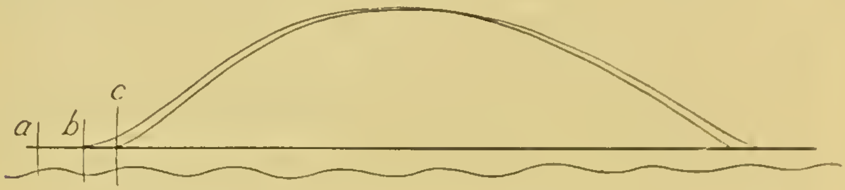


Fig. 154.—Two Single Muscle Curves.

a, Point of stimulation; *b*, instant at which contraction took place with the electrodes in the first position; *c*, when the electrodes were in the second position. Time tracing, 100 per second.

temperature is approached. The velocity of transmission in the human subject may be measured by comparing the length of the latent periods in records of contractions of the flexors of the thumb

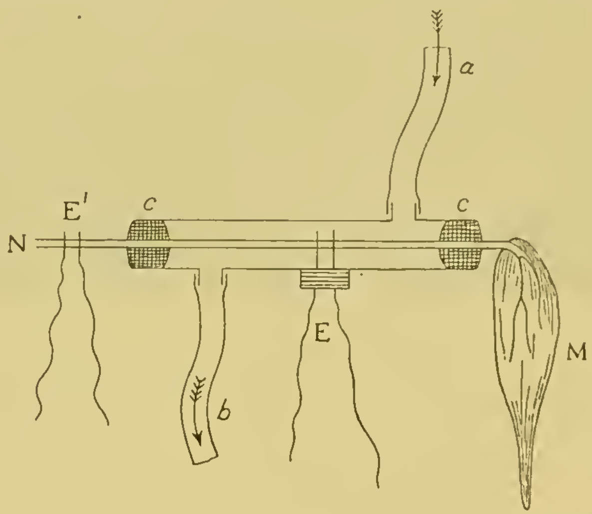


Fig. 155.—Apparatus for Testing the Action of Gases on the Excitability and Conductivity of Nerve.

a, Inflow tube; *b*, outflow tube; *c*, tube plugged at each end with normal saline clay through which the nerve passes; *E*, electrodes testing the *excitability* of the nerve, *N*, while under the influence of the anæsthetic; *E'*, electrodes testing its conductivity; *M*, muscle.

or fingers on stimulation (1) of the brachial plexus at the axilla, and (2) of the ulnar or median nerve at the elbow.

Temperature, as already indicated, has a marked influence on the rate of transmission; thus it may be reduced to even $\frac{1}{10}$th in the case of frog's nerve (Helmholtz).

The voltaic current when strong enough acts as a block; when weak, the rate of transmission (like the conductivity) is not much affected, being raised in the region of the kathode and depressed in that of the anode.

Co_2 and cocaine though suspending the excitability of a nerve do not suspend conduction.

Double conduction in nerves.—When a nerve is stimulated with electricity, we have seen that the impulse flows in both directions along the fibres, but in the living body the nerve fibre only transmits impulses in one direction. Instances of *double conduction* outside the body may be found in the diphasic current of action of nerve already studied, and also in Kuhne's gracilis experiment. The two parts of this muscle are supplied by two twigs from a common nerve which divides as it reaches it; and stimulation of either twig causes contraction of the whole muscle. It seems here as if the excited fibrils in the nerve fibre of the one twig conveyed impulses upwards till they joined the parent fibre above the point of division, when the impulse was communicated to adjacent fibrils destined to pass into the other twig.

Velocity of the electrical change that accompanies a nerve impulse.—The negative variation or current of action travels at the same speed as the nerve impulse, *i.e.*, about 90 feet per second in the frog (28 metres). (For method of estimating velocity, see "Differential Rheotome," page 133.)

Ritter's tetanus.—If the nerve of a nerve-muscle preparation be subjected to a strong constant current (ascending) for a few minutes, there is contraction at closing, and during the passage of the current there may be spasmodic contraction (closing tetanus) or galvanotonus, or the muscle may simply remain relaxed; on opening the current there may be a single twitch or some degree of tetanus (opening, or Ritter's, tetanus). If the nerve be divided between the electrodes, it still continues; but if between the anode and the muscle, it at once ceases, showing that the excitation was in the region of the anode.

Chemistry of nerve tissue.—Of the chemistry of nerve tissue we know little, and of the chemical changes taking place in the functionally active fibre still less. The analysis of the composition

of nerve fibres is usually made from the white matter of the brain, as the connective tissue element is there present to a very slight extent. The following is the result of the analysis :—

Water		68 per cent.	
Solids	Proteids	8 "	32 per cent.
	Cholesterin	16 "	
	Lecithin	3 "	
	Cerebrin	3 "	
	Salts	0·5 "	
	Other substances,	1·5 "	
		100	

Living nerve is neutral or slightly alkaline; dead nerve is acid in reaction.

The axis-cylinder probably resembles in its composition other forms of protoplasm, and contains *albumin* and *globulin*. Of the medullary sheath, *cholesterin*, probably combined with some of the fatty bodies, forms a considerable part. *Lecithin* and *cerebrin* are two of the fatty substances found, and also *neurin*, which differs from an ordinary fat in containing nitrogen. By some these are regarded as decomposition products of a still more complex fat, *protogon* (see page 20). *Xanthin* and *hypoxanthin* in small quantities are obtained from nerve. When all the fatty material has been dissolved out from the medullary sheath, a network of *neuro-keratin* is still left. The neurilemma is insoluble in dilute sodium hydrate. The connective tissue of the nerves yields *gelatin*.

CHAPTER V.

THE PHYSIOLOGY OF THE HEART.

THE blood-vascular system includes the heart, arteries, capillaries, and veins, and the blood contained in them. Through these channels the blood is circulated through every tissue of the body, to which it brings new material, and whence it carries effete products to be excreted by some organ specially differentiated for the purpose. The heart may be regarded as a four-chambered pump, from which the blood is sent by the aorta and pulmonary arteries, springing from the left and right ventricle respectively, through the *systemic* vessels to the body generally, and through the *pulmonary* to the lungs; while the other two chambers, the auricles, receive it back after it has completed its circuit. The course of the blood may be followed starting from the left ventricle. The blood leaves the left ventricle by the great *systemic* vessel, the aorta, and is distributed to every part of the body by repeated branching of the arterial tree, until ultimately the capillaries are reached.

Fig. 156.—DIAGRAM OF GENERAL COURSE OF THE CIRCULATION.

RA, Right auricle; *LA*, left auricle; *RV*, right ventricle; *LV*, left ventricle.

After passing through these, in which it comes into close relations with the tissues, parting with nutritive and receiving waste substances, it is collected by the veins and returned by the superior

and inferior venæ cavæ to the right auricle. It then passes into the right ventricle, which it leaves by the pulmonary artery to enter the lungs, which thus receive venous blood. The blood passes through the capillary network of the lungs, whereby it becomes oxygenated and rendered arterial, and is collected by the pulmonary veins, by which it is carried to the left auricle, and so to the left ventricle. It must be borne in mind, however, that the contraction of the two ventricles is synchronous, as is also that of the auricles, so that the circulation of the blood is carried on through both the systemic and pulmonary systems at the same time.

The portal and lymphatic systems are both virtually loops upon the systemic.

The study of the circulation involves the consideration of two classes of phenomena—those which are *mechanical*, and may be demonstrated by mechanical models, and those which are *vital* and dependent on the special qualities of a neuro-muscular apparatus; but no sharp line can be drawn between the two as they are so much associated and inter-dependent.

We may first consider the mechanical properties of the heart and blood-vessels. We are here dealing with an elastic hydraulic apparatus, which is virtually a pump (with valves) upon a system of closed elastic tubes. The contracting ventricle driving the blood into the aorta is the pump, the elastic tubes the vessels through which it flows. A model may readily be constructed in which an elastic syringe represents the heart, a piece of india-rubber tubing the arteries, joined by several smaller connecting tubes, the capillaries, with another piece to represent the veins.

The elasticity of the tubes is of the first importance, as it is through this and the resistance in the arterioles and capillaries that the flow of blood ceases to be intermittent and becomes constant. When water is forced by a pump into a rigid tube, the same amount escapes from the one end of the tube as enters it at the other, and at the same time ; in other words, the space within the tube is constant, and if the inflow be intermittent the outflow is too. If an elastic tube be substituted for the rigid one, it is found that the flow is still intermittent, because the fluid practically escapes as fast as it gets in. But if the outflow end of the tube be now partially constricted, an entirely different state of things supervenes. There is now *resistance* to the outflow, and the elastic nature of the wall of the tube enables it to expand in proportion to the resistance and the force of the pump, and so to accommodate a greater amount of fluid than the rigid tube could. The consequence of this is that the fluid is heaped up in the tube behind the point of constriction

to such an extent that when the contraction of the elastic pump is over the tendency of the walls of the tube to contract continues to act upon the fluid contained in it, and so keeps up a flow from the outlet, which is now continuous and not intermittent. In other words, enough fluid is sent into the tube with one stroke of the pump to maintain the outflow during the stroke and in the interval between it and the next, *i.e.*, during the systole and diastole of the heart. Of course there are many intermediate stages between complete intermittence and continuousness, the stage depending on the force and frequency of the propulsion, and the amount of restriction of the outflow. These vary inversely—that is to say, the less restricted the outflow the more frequent the propulsion of fluid requires to be, and *vice versa*. Now, the point in the vascular system corresponding to the restricted outlet of the indiarubber tubing is the arterio-capillary junction, the region of the small arterioles and the capillaries in which they end, and at this point the flow, which has been intermittent in the arteries (causing the pulse), becomes continuous and remains so through the capillary and venous channels.

As the arterial wall is either being distended by the projection of blood into the vessel from the ventricle, or contracting upon the blood sent into it after the ventricular systole is over, it follows that the blood exerts a certain lateral pressure upon the arterial wall, and this is readily estimated by the introduction of a vertical glass tube into one of the vessels, say the carotid. We shall return to the details of the experiment later: at present we may neglect the means adopted to prevent the coagulation of blood in the tube, loss of blood, errors in estimation, &c. In such a tube the blood rises immediately after its introduction with every beat of the heart, to a progressively diminishing extent, until it reaches, in a small mammal such as the rabbit, a height of about 3 feet, or 90 cm., when it has attained its maximum and oscillates about a mean level, rising above it with the systole of the ventricle, and falling below it during the diastole. The pressure in the artery, called the *blood-pressure*, is now balanced by the column of blood, and is therefore said to be equal to 3 feet, or 90 cm., of blood, or 70 mm. of mercury.

If a similar experiment be performed upon arteries further from the heart, and upon veins, it is found that the pressure falls, but in the case of arteries the oscillations, though smaller, still take place above and below a mean level; while in veins, where the fall of pressure is still greater, no oscillations occur, showing that the pressure is now constant—in the jugular of the rabbit about 3 to 4 mm. of mercury. Also, the pressure in the veins is greatest towards

the periphery, and falls as the heart is approached. The capillary pressure cannot be measured in this way, but by finding the amount of pressure necessary to prevent the blood entering the capillaries and small vessels of the web of the frog's foot, for example, it can be shown to be here about 7 to 10 mm. of mercury, and in mammals 20 to 30 mm.

A diagram may be made of the mean pressure from the aorta to the vena cava, showing a continuous fall from the aorta to the capillary region (region of small arterioles, capillaries, and venules —"peripheral resistance" area), a very sudden and pronounced fall in this region, and again a slower, more gradual fall in the veins. The pressure is greater in the artery near the heart than at a distance from it, because some of the pressure at this point has been used in propelling the blood to the further point; and similarly

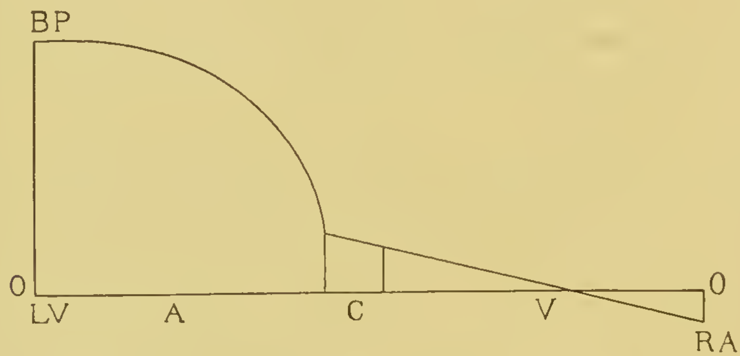


Fig. 157.—Scheme of Blood-Pressure.

Showing the amount in left ventricle, arteries, capillaries, veins, and right auricles. *O O*, Line of no pressure.

the pressure near the periphery in a vein is greater than it is in the same vein near the heart, because some of the pressure near the periphery is used in driving the blood towards the heart.

The aorta divides again and again before it reaches the peripheral region, as a tree does between the stem and the terminal branches, and the sectional area of its ultimate subdivisions is much greater than that of the vessel itself; but the narrowness of the passages represents an enormous increase of friction, and this increase constitutes the peripheral resistance and enables advantage to be taken of the elasticity of the vessel wall, and the blood to be heaped up on the cardiac side of it. As far as the sectional area is concerned, however, the arterial channel may be represented as a cone, the apex of which is at the heart and the base at the arterio-capillary boundary. Similarly the sectional area of the

venous system is greatest at the tissue commencement and least at the heart; so that the whole circuit may be represented by two cones placed base to base, the bases representing the capillary region and the apices the commencement or termination of the large vessels in the heart.

We may now return to the model or schema of the circulation, and see if we can demonstrate the principal phenomena in a purely mechanical manner.

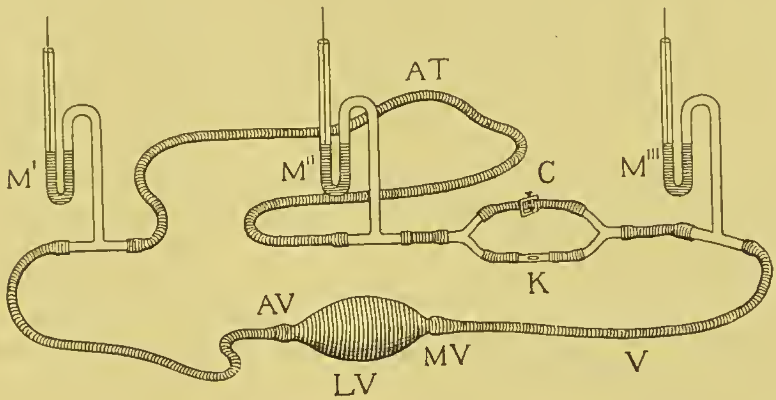


Fig. 158.—Scheme of the Circulation.

The Syringe LV represents the left ventricle; AV, the aortic valves; the tube AT the arterial tree; M^{I}, a manometer near the heart; M^{II}, a manometer near the periphery; C, an open connecting tube with a clamp upon it; K, a connecting tube with tow or sponge in it; the tube V the large veins, upon which is placed a manometer M^{III}; MV, the mitral valve.

Let a manometer for registering the pressure be placed upon the tube representing the artery and another on that representing the vein. The manometer may be conveniently one of mercury in an S-shaped tube, a float being placed upon the surface of the mercury in the open end, bearing a light rod arranged to write on a moving surface. The connecting tubes between the arterial and venous trunks may be two in number, one of them being fitted with a clamp and the other containing tow or sponge. When the first is allowed to remain patent there is nothing to represent peripheral resistance, as the fluid flows freely through it; when clamped the fluid passes through the tube containing the sponge or tow and resistance is established. If, with the tube unclamped, we now squeeze the syringe by hand at regular intervals, the mercury in the proximal (arterial) manometer rises, then falls, and this is followed by a similar rise and fall in the distal (venous) manometer. The

absence of any restriction of the flow between the two main tubes enables the fluid to leave the arterial tube as quickly as it enters it, so that no mean pressure is established; and as the fluid passes on into the venous tube under similar conditions (for there is no restriction of the outflow from it), the same rise and fall of the mercury in the corresponding manometer takes place, though the height to which the mercury rises is less, as the pressure of the fluid falls the further the point is from the propelling force.

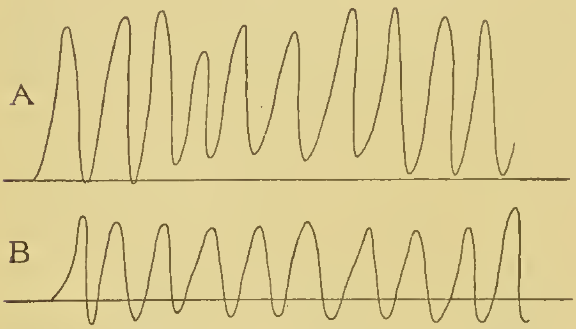


Fig. 159.—Tracings Taken from a Schema in which the Peripheral Resistance was Slight.

A, Arterial manometer; *B*, venous manometer.

The record on the moving surface under these conditions will be somewhat as shown in Fig. 159, in which A represents the tracing from the arterial manometer, and B that from the venous. If the connecting tube be now clamped, and peripheral resistance thrown in thereby, as already explained, another series of events follow periodic contraction of the pump. The mercury in the arterial manometer will rise with each contraction but fall to a less extent until a mean pressure is attained, about which oscillation of the mercury continues to take place. The mercury in the venous manometer will also rise

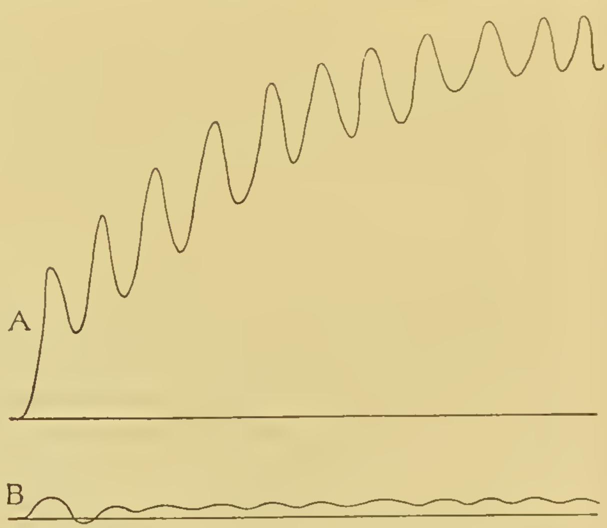


Fig. 160.—Tracings from a Schema with the Peripheral Resistance High.

A, Arterial manometer; *B*, venous manometer.

to a certain lower mean level, but will show only slight oscillations, as it is no longer directly influenced by the stroke of the pump, the intermittency of the flow having ceased at the peripheral resistance. The record under these conditions is shown in Fig. 160, in which the rise up to the mean level of the arterial pressure is well seen.

The *rate of flow* through the vessels is greatest in the aorta, and decreases outwards until the capillaries are reached, in which it is slowest of all. The speed increases again in the veins and grows greater as these approach the heart—that is to say, the rate of the flow varies inversely with the total sectional area of the channels traversed. The entire circuit occupies about a minute. About half-a-second is spent in the capillaries of the tissues, and another half-second in those of the lungs.

The **structure of the heart.**—The heart is enclosed in a serous sac, the pericardium, which, like those of other organs, has a visceral and a parietal layer, which meet about the roots of the great vessels. The visceral layer (sometimes called the *epicardium*), which gives the smooth glistening appearance to the surface of the heart, consists of a layer of polygonal, squamous cells superficially, with a basis of connective tissue beneath, containing blood-vessels, lymphatics, and nerves, continuous by its deeper surface with the connective tissue between the muscular fibres of the myocardium. The *myocardium*, or muscular substance of the heart, is arranged in a series of layers disposed in a whorl-like manner. Its intimate structure has already been described under the heading of "Cardiac Muscle" (see "Simple Tissues"). The muscle cells are somewhat quadrangular when seen lengthwise, having serrated ends by which the cells in a fibre are cemented to each other. Each cell has an oval nucleus near to the centre, and granules of pigment may usually be seen in the cell substance at its poles, especially in old people. The cell body is short and gives off a branch obliquely, the serrated end of which joins that of another branch running in the opposite direction from a cell in an adjacent fibre, and in this way a very complete network is formed. Between the cells, in the meshes of the network, is found connective tissue supporting blood-capillaries and lymph channels and nerve fibres. The *endocardium*, or lining membrane of the heart, closely resembles the pericardium, but is much thinner. It consists of a layer of polygonal, squamous cells with a thin stratum of connective tissue beneath it, continuous with the connective tissue of the myocardium. Unlike the intima of the arteries the endocardium is vascular.

The veins of the heart, with the exception of the coronary sinus (valve of Thebesius), possess no valves. The Eustachian

valve at the opening of the inferior vena cava never closes the opening, but in the fœtus helps to guide the blood through the foramen ovale into the left auricle. But in place of valves the veins have a special ring of muscular fibres around their openings, which, by their contraction at the onset of the cardiac systole, serve the same purpose and prevent the regurgitation of blood backwards. The auricular contraction commences at these rings and spreads from them over the appendices and auricles generally, until the blood is driven into the ventricles. When the blood has passed into the ventricles the valves between them and the auricles close, and prevent regurgitation into the auricles.

When the ventricles contract, the blood is driven into the aorta and pulmonary artery, and the sigmoid valves then close, preventing its return. The *sigmoid valves* are plications of the endocardium, the free margins of which are directed away from the heart, their attached margins being continuous with the fibrous ring uniting the aorta or pulmonary artery to the ventricle from which it springs. They have three cusps which are semilunar in shape and composed of a sheet of connective tissue covered on either side with a layer of polygonal squames. Blood-vessels are found in the cusps, except in the lunule, the thinner free border, in the centre of which is found the corpus Arantii — a small thickening of connective tissue, which completes the closure of the valve in the middle when the cusps come together. The *auriculo-ventricular* valves are also folds of the endocardium, continuous with the fibrous rings uniting the ventricles and auricles, into the cavity of the former of which they project. Their somewhat triangular cusps are united to the fibrous ring by their bases, and give off from their sides the chordæ tendineæ, and these join the musculi papillares of the ventricular wall, which indicate, perhaps, the remnant of an early condition of the mammalian heart, comparable to the sponge-like framework of the frog's. The cusps are covered on each side with squames, and consist of a basis of connective tissue supplied with blood-vessels. The chordæ tendineæ, springing from one projection of muscle substance, are attached to the adjacent sides of two cusps, and not to the two sides of one. The mitral valve between the left auricle and ventricle is bicuspid, that between the right auricle and ventricle tricuspid. The function of the chordæ tendineæ is to hold the cusps in position and prevent them being carried back into the auricles when the ventricles contract, and this would still be liable to happen were it not for the musculi papillares. Contraction of the ventricular wall leads to a diminution of the ventricular cavity, and hence the origin and insertion of the chordæ tendineæ are brought closely

together, and the cords themselves would become slack; but the musculi papillares, by themselves contracting at the same time as the ventricle, shorten, and so compensate for the decrease in diameter. But if the ventricle be over-distended so that the diameter is greatly increased, the chordæ tendineæ may even prevent the cusps meeting and so lead to regurgitation into the auricle; and this sometimes occurs in cases of dilatation of the right ventricle.

The **cardiac cycle.**—The movements of the heart are rhythmical in character, and the two sides act synchronously. In studying the events occurring in the cycle we may therefore take either side, and what is said will apply equally well to the other in essential points. Previous to the systole, the blood is flowing quietly along the venæ cavæ to the right auricle. The auricular contraction is preceded by a wave passing along the venæ cavæ in the neighbourhood of the heart in a peristaltic manner, until it involves the rings of muscular fibres around their openings. When these rings contract, the blood in the auricle is shut off from the veins, and the contraction wave, spreading quickly to the auricular wall itself, causes the cavity to be obliterated and the blood to be poured into the ventricle. As the blood is passing into the ventricle it sets up an "eddy-stream" behind the cusps of the auriculo-ventricular valve, which floats them up, and either closes them before the ventricle contracts, or leaves them in the most favourable position for the intra-ventricular pressure to act upon them and secure their closure when contraction takes place. Then follows the ventricular systole, closing or rendering more tense the tricuspid valve, the segments of which are held in position by the chordæ tendineæ, in spite of the contraction of the heart wall, through the compensating action of the musculi papillares. The edges of the segments are extremely thin and fall into apposition with each other, much as the lunules of the semilunar cusps of the sigmoid valves do, and thus secure more complete closure. As the ventricle contracts it forces open the semilunar valve at the orifice of the pulmonary artery, which has hitherto been kept closed by the presence of the blood in that vessel, and here again, as the blood pours through the orifice past the valves, an eddy-stream is set up—a reflux—which prevents the flaps of the valve being brought against the wall of the vessel. This is helped, too, by the anatomical peculiarity of the part, the arterial wall bulging outwards opposite each cusp, the space being called the sinus of Valsalva. (In this way, in the aorta, the opening of the coronary artery is saved from occlusion during the systole of the ventricle, and no doubt receives its supply of blood the first among the vessels given off from the great systemic trunk). When

the ventricle has completed its contraction it suddenly relaxes, and a reflux, caused mainly by the elastic recoil of the artery, takes place, which brings the semilunar cusps together, their lunules being closely applied to each other, the corpora Arantii meeting in the centre. Thus, in the closing of both the auriculo-ventricular and sigmoid or semilunar valves, the strongest part of the cusps bears the main strain, while the thin free borders are applied to each other to render the closure more complete. The systole of the ventricle is succeeded by a *pause* before the auricle contracts again. Thus the three events of the cycle are—(1) Auricular systole; (2) ventricular systole; (3) pause. All that has been said of the cycle of events on the right side of the heart will apply also to the left, anatomical differences being borne in mind, and also that the intra-ventricular pressure in systole is much greater on the left.

Certain changes in the form of the heart take place during the systole. In diastole the cross-section of the base of the ventricles is roughly an ellipse, the long diameter being from side to side; but the ellipse is more convex in front than behind. On contraction the side to side diameter is much reduced, and the antero-posterior increased, so that the section now is more nearly circular. The long diameter seems to undergo little alteration, though by some it is regarded as slightly shortened. With the systole the auriculo-ventricular orifices also contract, and so increase the efficiency of the valvular arrangements. The number of heart beats per minute is about 70 to 75 in man, and the duration of the events in the cardiac cycle is as follows:—The auricular systole occupies $\frac{1}{8}$, the ventricular $\frac{3}{8}$, and the pause $\frac{4}{8}$ of the whole period. In a rapidly-contracting heart, the pause is more shortened than the systole.

The movements of the auricle and ventricle of the frog's heart, and the pause, may be conveniently demonstrated by an arrangement of levers bearing mirrors (one for the auricle and another for the ventricle) which cast two spots of light upon a screen. The mirror light of the auricle moves first, and is immediately followed by that of the ventricle, and this by the pause. The effect of heat and cold upon the heart is easily shown in this experiment, the mirror movements following each other more rapidly under the application of heat, and more slowly, the pause being lengthened, when the temperature is lowered.

The events of the cardiac cycle may also be recorded graphically on a moving surface through Chauveau and Marey's *heart sound*. This instrument (Fig. 165) consists of a tube with an elastic bag at one end for the ventricle, and another in the course of the tube,

at a suitable distance from the first, for the auricle. The bags each communicate by separate divisions of the tube with a tambour and lever, the two levers being arranged to write, the one beneath the other, on a revolving drum. The heart sound itself is introduced through the jugular vein of a large animal, such as the horse, into the heart, the bag at the end being in the right ventricle, and the one at a little distance from it in the auricle. When the latter contracts, the lever connected with it rises and then falls, and this is succeeded by the rise of the ventricular lever and its fall, and

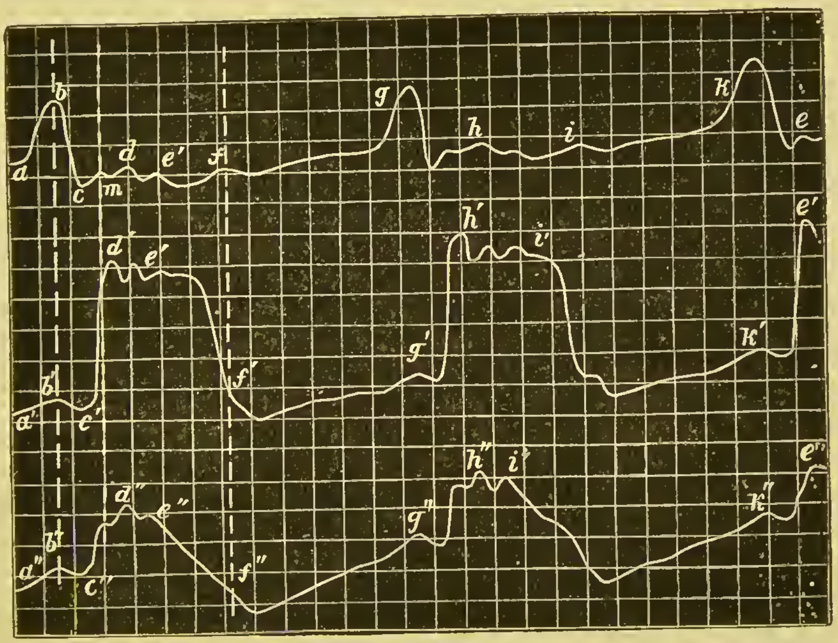


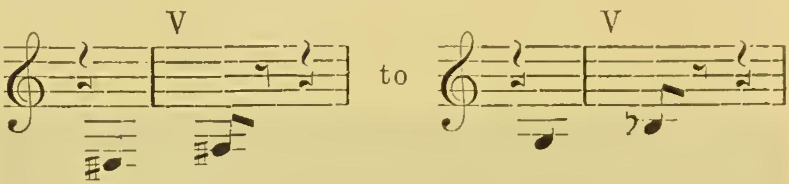
Fig. 161.—Tracing obtained from the Heart of a Horse.

The upper tracing is from the right auricle, the middle from the right ventricle, and the lowest from the apex of the heart. The horizontal lines represent time, while the vertical represent the amount of pressure. The vertical dotted lines mark coincident points in the three movements. The breadth of one of the small squares represents the one-tenth of a second.

this by the pause before the auricle begins again. The instrument is not suitable for the purpose of accurate measurements of pressure, but is useful for showing the events of the cardiac cycle graphically. It can be used upon the left side of the heart if introduced through the carotid artery, and tracings from the left ventricle and aorta thereby obtained.

The **cardiac sounds.**—Of the two cardiac sounds, the first commences with the closure of the auriculo-ventricular valves and

lasts up to, or nearly up to, the end of the systole of the ventricles; the second commences with the closure of the semilunar valves, and hence corresponds with the commencement of the diastole or pause. The first sound is dull and booming in character, the second shorter and sharper, and they are likened to the words *lūbb*, *dŭp*, or the sound may be expressed thus :—



The relation of the sounds to the events of the cardiac cycle is shown in the accompanying figure, in which, however, it will be seen that the time relation of the three events is not the same as that already given. Here the auricular occupies much less of the whole systole. The cardiac sounds are readily heard when the stethoscope is applied to the chest wall, especially in the region of the cardiac impulse. The second is undoubtedly due to the stretching and vibration of the sigmoid valves when the blood presses upon them at the beginning of the diastole. It disappears if the cusps are hooked back so that they cannot meet, and it is altered in character to a murmur if the valves are diseased. The sound is heard most distinctly at the level of the second right costal cartilage at its junction with the sternum, in fact at the point where the aortic arch most nearly approaches the chest wall, and is due

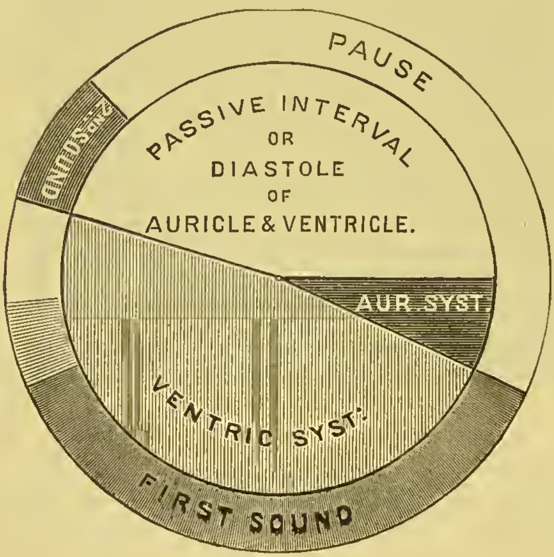


Fig. 162.—Scheme of a Cardiac Cycle.

The inner circle shows the events of the cardiac cycle; and the outer the time relation of the heart sounds to the events.

to the stretching and vibration of the aortic valve, and to a lesser extent to that of the pulmonary artery. The sound produced by the latter is best heard in the second intercostal space on the left side, close to the sternum.

The cause of the first sound is not quite so clear. It is heard most distinctly in the region of the apex beat, and any alteration by disease of the mitral valve is also heard here most distinctly. Should the tricuspid be injured the alteration in the sound is heard most readily over the ensiform cartilage. The question arises—Is the first sound due to the muscular contraction of the ventricles, or to the stretching and vibration of the auriculo-ventricular valves, or to both? and the last is probably the correct view. In the excised, bloodless heart, the sound is still heard, and here obviously cannot be due to stretching of the valves. Though the contraction of the heart is not tetanic but a prolonged simple contraction, if we adopt the view that the note of muscle is not produced by a repetition of many simple contractions per second, but is due to alterations in tension during contraction, whether simple or compound, there is no bar to the simple contraction of the heart producing a muscular sound. It has been said in favour of the view that the valves alone are concerned in the production of the sound, that this is replaced by a murmur when the chordæ tendineæ are cut, and altered or even made to cease if the larger veins be clamped; yet both these conditions would alter the tension of the heart muscle during contraction as well as affect the valves, and do not therefore show that the ordinary muscular tension during contraction is not contributory to the sound. Furthermore, the booming character of the first sound is in support of the idea that it is not due to the tension of the valves only, as in the case of the second sound. That the cardiac impulse contributes to the sound seems improbable, as it is heard equally well when the chest wall is removed.

The locality where the sounds are best heard depends upon conduction. Thus, in the case of the first sound, we should expect any sound produced, more especially in the left ventricle, to be conveyed to the chest wall at the point where the apex strikes it, and this is found to be the case; and it is so with the other sounds. The sound produced by the tricuspid valve is heard most readily in the region of the ensiform cartilage—a little to the right of it.

In some cases in which the action of the heart is not completely synchronous, the aortic and pulmonary sounds are separate, *i.e.*, the second sound is "reduplicated." A presystolic murmur arises if there be any obstacle to the passage of the blood from the

auricle into the ventricle; when, for instance, there is stenosis of the mitral valve.

Endocardiac Pressure.

The endocardiac pressure, *i.e.*, the pressure in the cardiac cavities, may be estimated by means of a cannula connected with a mercurial manometer, as in the case of arterial blood pressure. But the rapidity of the changes of pressure in the heart and the inertia of the mercury render a tracing obtained in this way imperfect, and some modification becomes necessary to overcome these difficulties. So far as we are concerned with the determination merely of the highest and lowest pressure attained in any cavity, this is readily obtained by the introduction of a ball and socket valve between the heart and

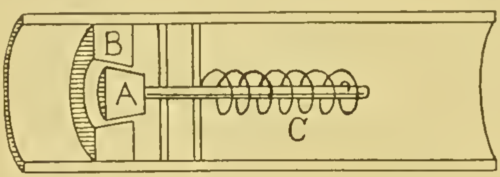


Fig. 163.—Gaule's Maximum and Minimum Manometer, constructed on the Principle of a "Ball and Cup" Valve.

A, ball; *B*, cup; *C*, spring. When the spring is directed towards the heart it acts as a maximum manometer, when away from it as a minimum manometer.

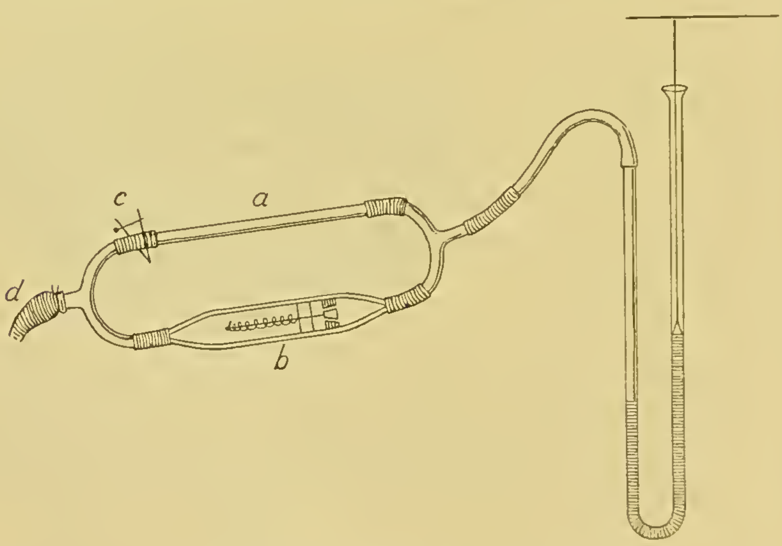


Fig. 164.—Maximum Manometer.

d, Connection with tube going to heart; when clamp *c* is closed the valve *b* comes into play, and the instrument acts as a maximum manometer. If *c* is opened *a* becomes patent and conveys the variations and pressure, the instrument then acting as an ordinary manometer.

the manometer; the apparatus being so constructed that the valve may be adjusted to act either way. When arranged so that it will admit of the passage of fluid from the heart but not in the opposite direction, the manometer becomes a *maximum* one, *i.e.*, it records the greatest height only to which the mercury is raised, as the fluid cannot pass back; and when arranged so that the fluid can only pass towards the heart, and not from the heart into the vessels, it becomes a *minimum manometer* and records the lowest level to which the mercury has fallen during the cardiac cycle. It will be obvious that this manometer gives us no tracing that is of value in determining the various changes of pressure and the points in the cardiac cycle at which they take place, but only the highest and lowest pressures reached during the whole cycle. In this way the pressure in a dog's heart has been recorded as follows:—

	Maximum pressure.	Minimum pressure.
Left ventricle,	140 mm.	— 30 to — 40 mm.
Right ventricle,	60 "	— 15 "
Right auricle,	20 "	— 7 to — 8 "

It will be observed that in each of these three cavities the pressure falls at some point appreciably below that of the atmosphere—that is to say, the mercury is drawn back towards the heart.

In obtaining tracings of the endocardial pressure which may show the maximum and minimum pressure with some accuracy, and also the changes in the pressure and their relation to other events of the cardiac cycle, it is necessary to discard the use of the mercurial manometer on account of its inertia, and various other manometers have been employed. To one of them, Chauveau and Marey's, allusion has already been made. Here we have an arrangement, the essence of which consists in an elastic tube connected at one end with a tambour and at the other with a cannula or tube, terminating in an elastic ampulla. When the heart contracts, the air in the ampulla is forced along the tube to the tambour, the lever connected with it is raised, and a curve described. By using two tubes, one connected with the auricle and the other with the ventricle, the tracings may be recorded simultaneously on a moving surface. Instead of two entirely separate instruments being used the two elastic tubes may join a double cannula with one ampulla at the end and the other at an appropriate distance, so that when the first is

in the ventricle, the second is in the auricle. The cannula is introduced through the large vessels. Fig. 161 shows a tracing obtained in this way of the pressure in the right auricle and ventricle, and beneath this a tracing of the *cardiac impulse* by the application of the same principle. The instrument used for this last tracing is the *cardiograph,* which consists of a round box closed at one end with a membrane, from the centre of which a button projects, which is pressed upon the point where the heart strikes the chest wall; while the other end of the box is connected with a tube passing to a tambour with a writing lever.

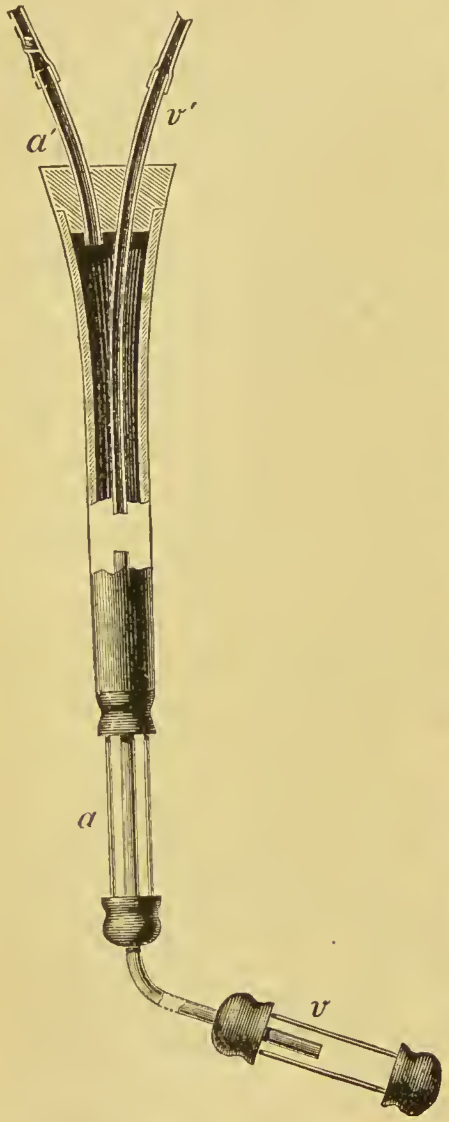


Fig. 165.—CHAUVEAU AND MAREY'S HEART SOUND.

v, Ventricular, and *a*, auricular ampulla; *a′*, tube connected with auricular ampulla; and *v′*, tube connected with ventricular ampulla.

But though Chauveau and Marey's method of recording the changes of pressure during the

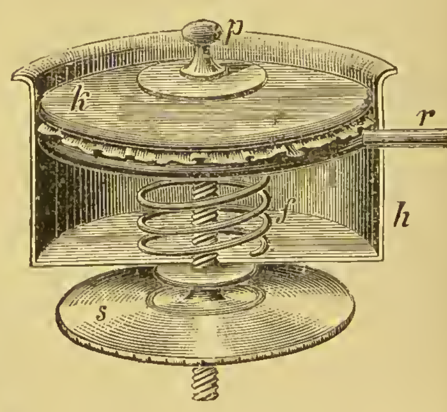


Fig. 166.
MAREY'S CARDIOGRAPH.

p, Button applied over point of cardiac impulse; *k*, membrane of tambour; *r*, tube connected with tambour and writing lever; *f*, spring; *h*, metal box; *s*, graduating disc.

cardiac cycle has its value, it has also serious disadvantages. In the first place, the relative pressure in the auricle and ventricle is

not, as will be seen in the figure, in accordance with the result obtained by means of the maximum and minimum manometer, as the auricular ampulla has been purposely allowed to be more sensitive in order to give a more marked result; and though careful graduation may remove this particular objection to a large

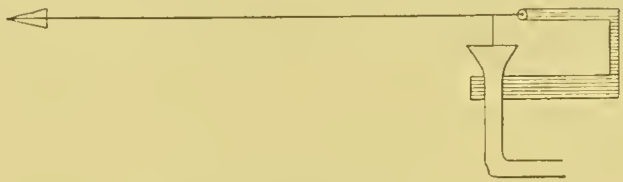


Fig. 167.—Diagram of Hürthle's Manometer. (See also "Fick's Spring Manometer.")

extent, the result is not wholly satisfactory. The length of the tube also, the tendency of the tambour to record inertia vibrations of its own, and the fact that only the *positive* pressure is recorded by this instrument, combine to render it imperfect and insufficient when accurate detail is required.

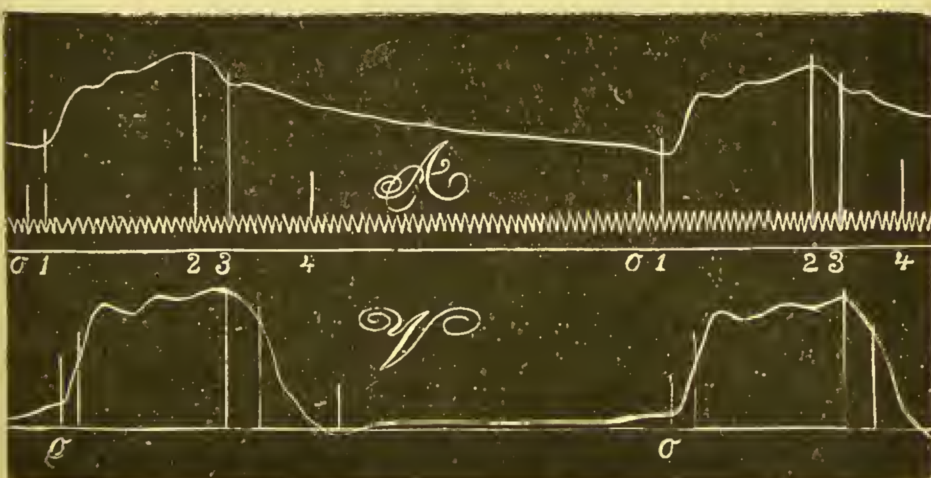


Fig. 168.—Simultaneous Record of Pressure in Left Ventricle (V) and Aorta (A) (Hürthle).

Tracings taken with elastic manometers: *O*, indicates a point just before the closing of the mitral valve; 1, the opening of the semilunar valve; 3, the closure of the semilunar valve; 4, the opening of the mitral valve. The ventricular curve shows a "plateau."

In the manometer now in use for recording the quickly changing endocardial pressure, the blood works against the torsion of a spring instead of the weight of a column of mercury. In Hürthle's *spring manometer* a cannula connected with a short tube

is passed into the heart through the great vessels, the other end of the tube joining a small tambour, which works by means of a button upon a spring connected with a lever. The tube and cannula are filled with saline solution to prevent coagulation, the tambour being either filled with the same solution at the same time, or allowed to remain filled with air. The tracings obtained by this instrument differ according to whether air or fluid is thus allowed to be the medium of the transmission of the pressure.

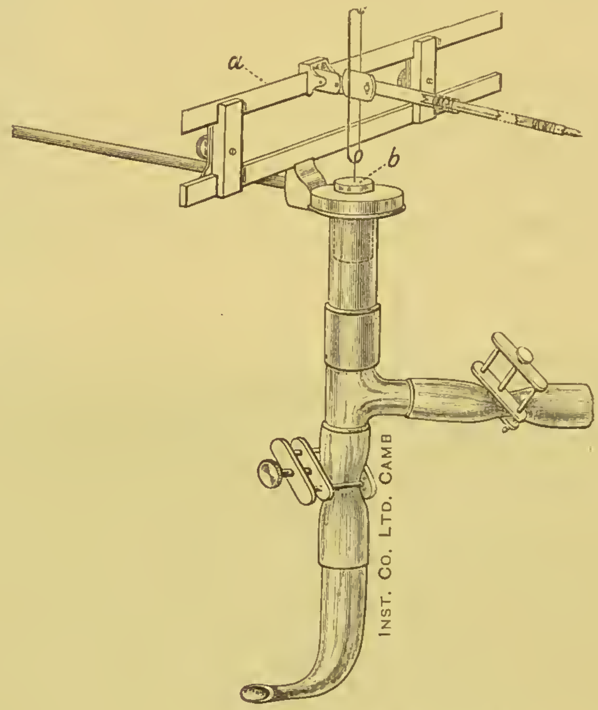


Fig. 169.—Roy's Torsion Manometer.

The movements of an ebonite piston, *b*, in a brass cylinder twist a strip of steel, *a*, and at the same time are magnified by a recording lever.

When fluid is used the ventricular tracing reveals a tolerably well-sustained *plateau* after the sudden rise; when air is employed the ventricular tracing is peaked.

Another instrument for recording the pressure changes is that devised by Roy and Rolleston, in which the blood (through an intermediate saline solution) works upon a readily movable piston connected with a lever, the two working against the torsion of a

steel ribbon. The connecting cannula may be introduced into the heart through the large vessels, or, as is more frequently done, a trocar may be passed directly into the ventricular cavity through the heart wall.

In a curve of the ventricular pressure taken by this instrument b' may be considered to mark the commencement of the systole of the ventricle. At c the sudden rise ceases and becomes converted into a fall, which is only gradual till the point d is reached. This gradual sinking in the level of the plateau is due to the passage of blood into the arteries, the pressure of the contracting ventricle being still sustained. From d to a there is a very sudden fall, due to the relaxation of the ventricle after its systole is over. Thus from b' to d represents the systole of the ventricle. At some part of the plateau a point, c', will be observed at which the descent becomes less marked than before, previous to the great drop after d. This point may indicate the time when the blood of the ventricle ceases to escape into the vessels, the portion of the curve

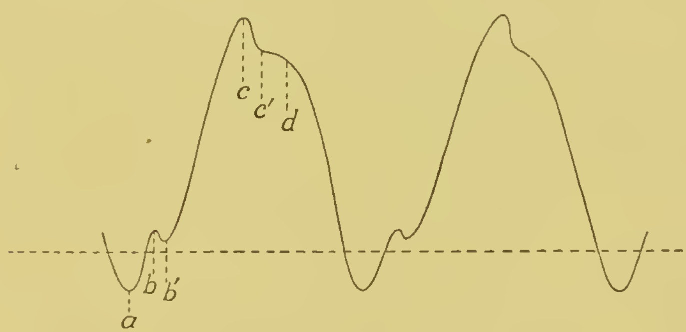


Fig. 170.—Curve of Ventricular Pressure.

between c' and d representing the still maintained contraction of the ventricle for a short period after it has completely expelled its contents. Sometimes the curve presents a small rise after c', causing a notch in the tracing, and by some this has been attributed to the closure of the semilunar valves acting on the ventricular pressure, but this is not distinctly proved. The smaller elevation in the tracing at b (before the sudden rise at b') is commonly attributed to the contraction of the auricle increasing the pressure in the ventricle.

According to Rolleston there is no distinct auricular contraction to be observed on the ventricular tracing; the auriculo-ventricular valves are closed in the lower third of the rise, from b' to c, and their closure gives rise to no notch; the semilunar valves open a little before c is reached and close a little before d.

We have yet to refer to the negative pressure during the diastole of the ventricle, shown by the dip of the curve at *a* below the abscissal line, which represents the atmospheric pressure. The cause of the negative pressure has been much discussed and may be due (1) to the action of the wall of the chest in inspiration, or (2) to the suction power of the relaxing and enlarging ventricle. As the negative pressure is still present (though diminished) when the chest wall is removed, the ventricular wall itself in expanding must be regarded as at least contributory to the production of the result. When the pressure changes from negative to positive this is due to the sudden contraction of the auricles forcing blood into the ventricles. In the right ventricle the negative pressure is trivial as compared with that of the left, and this we should expect if it were produced by the suction power of the expanding comparatively thin-walled chamber.

Duration of the phases of the cardiac cycle.—The more exact measurement of the various phases of the heart cycle may be given as follows:—Taking the usual rate of beat to be 72 per minute, the whole event would occupy ·8 second. Of this ·3 may be allowed to the ventricular systole, which, as we have seen, is divisible into three sub-phases—(*a*) rapid contraction, (*b*) emptying of contents into the vessels, (*c*) contraction maintained after expulsion of contents; and to each of these sub-phases ·1 second may roughly be allotted. We have now left ·5 second for the diastole of the ventricle, which exceeds the *pause* of the heart as a whole by the time occupied by the auricular systole preceding the ventricular contraction, and this again may be put at ·1 second. Thus ·4 second remains for the general pause of the heart, during which neither the auricles nor ventricles are contracting. The period of relaxation of the ventricles occupies ·1 second of this time, reducing the absolute period of rest to ·3 second. It must, however, be borne in mind that these figures can but be approximate, and that alteration in any one will necessitate a corresponding alteration in the others.

The **output of the heart and the work done.**—The *amount of blood* expelled from each ventricle during a contraction has been estimated at from 6 to 4 oz., or from 180 to 125 grams. According to Stewart, in a man weighing 70 kilos. it is as low as 105 grams per beat. Various methods for making these calculations have been adopted. The amount discharged from the aorta of a dog (when all the vessels but one have been ligatured) is collected into a receiver, measured, and divided by the number of beats

during the time of collection; or the capacity of the recently removed ventricle may be calculated by filling it with blood at a pressure equal to the average pressure in the ventricle. On the assumption that the ventricle completely empties itself at each contraction, this amount will represent the quantity ejected with each beat. And there are other methods (Stewart's, Zuntz's, &c.), into which we cannot here enter. Each ventricle necessarily ejects an equal amount of blood. The *work done* is determined by multiplying the amount of blood ejected by the height to which it is raised in a vertical tube; and if, in the case of the left ventricle, a column two metres in height is supported in a tube led from the aorta, the work of the left ventricle per beat will be 250 gram-metres, the output being taken as 125 grams. Taking the pressure in the right ventricle at one-fourth that of the left, 80 gram-metres, roughly speaking, of work may be added, making the total ventricular work per beat 330 gram-metres. The heart beating at the rate of 72 per minute, the work will amount in 24 hours to more than 30,000 kilogram-metres, or about a quarter of the work done by an ordinary labourer per diem.

The **cardiac impulse** is synchronous with the ventricular systole and is felt most distinctly in the fifth interspace, about an inch below the nipple and a little to the sternal side. It may also be felt, if an incision be made in the diaphragm from the abdomen, by introducing the fingers between the heart and the chest wall. It is mainly due to the sudden hardening of the ventricles when systole takes place, and to some extent also to the tilting forwards, and to the right, of the apex of the heart at the same time. A tracing may be taken of the impulse by means of the cardiograph already referred to, and it is found that the record thus obtained is not very different from that obtained by placing a lever on the exposed heart and recording its front to back movements during contraction. Such a tracing is termed a cardiogram. The significance of the various features of it is practically the same as in the tracing of endocardial pressure by Roy and Rolleston's method (Fig. 170).

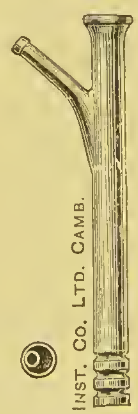


Fig. 171.—Perfusion Cannula for Frog's Heart, Consisting of a Double Tube, one inside the other. The Inner Tube Branches to the Left.

Tracings from the frog's heart. — The endocardiac pressure of the frog's heart may be studied and recorded by means of a

perfusion cannula connected with a mercurial manometer. The cannula is "two-wayed," *i.e.*, it consists of two tubes, one inside the other in their lower part, the upper ends being separated. The lower end is tied into the heart, after being introduced through an opening in the sinus venosus, by a ligature at the level of the auriculo-ventricular sulcus. Nutritive fluid allowed to pass into the free end of one of the tubes (inflow *a*) passes through the heart and is discharged by the other tube (outflow *b*). If *b* be connected with a mercurial manometer, the mercury in the open limb of which contains a float and style, the changes in endocardiac pressure may be recorded on a moving surface.

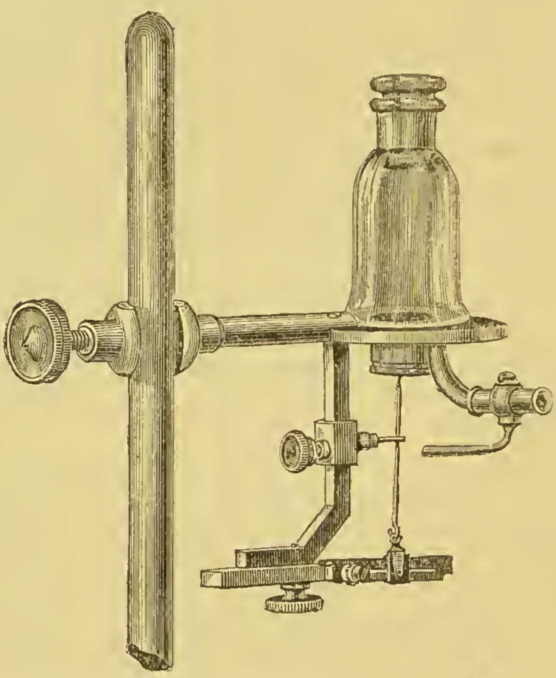


Fig. 172.—Roy's Tonometer for Measuring Changes of Volume during Contraction of the Heart.

The changes in volume in the heart of a frog during contraction and diastole may be recorded by means of Roy's tonometer. Here the heart is fixed upon a two-wayed cannula as before, so that fluid may be passed through it. The cannula is fixed in a stopper which closes the upper end of a bell-jar filled with oil, into which the heart is plunged. The lower end of the bell-jar is closed by a membrane connected with a lever. The bell-jar being completely filled with oil, at each contraction of the heart the

membrane, which is movable, rises and lifts the lever with it; and correspondingly on each dilatation it is depressed and the lever falls, a tracing being taken on a moving surface. It is thus the movement of the oil outside the heart that is recorded.

Schäfer's plethysmograph is constructed on the same principle. It consists of an air-tight vessel on a tube containing oil. The vessel receives the heart and the end of the perfusion cannula as

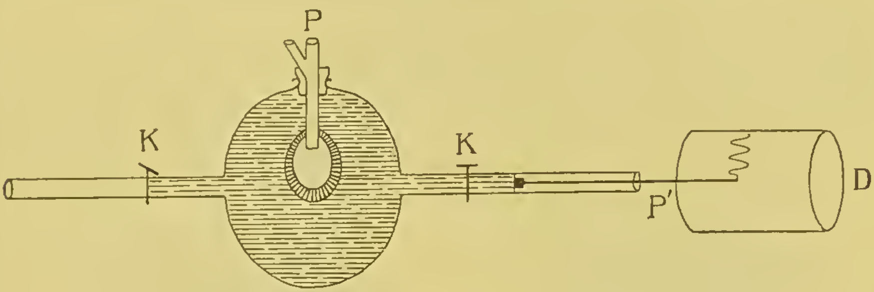


Fig. 173.—Schäfer's Plethysmograph.

K, Stop-cocks; *P*, "two-wayed" cannula connected with heart; *P*ʹ, writing lever; *D*, drum.

before. The glass tube at one end is closed by a stop cock, and the other contains a piston connected with a writing lever. As the heart contracts and expands, the piston approaches and recedes from it, and the lever attached to it records the tracing.

The movements of the frog's heart may be recorded in a still more simple way than those already mentioned, *i.e.*, by means of a lever alone. The lever may be adjusted so that it rests through

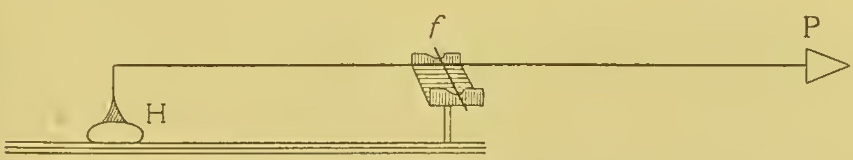


Fig. 174.—Principle of Lever for Frog's Heart.

H, Heart; *f*, fulcrum; *P*, writing point of lever.

an intermediate vertical support upon the surface of the heart, and it may readily be applied either to the ventricle or auricles alone, or upon the auriculo-ventricular sulcus; or instead of this a fine thread may be attached to the apex of the exposed heart of the frog and tied to the end of the lever. As the heart shortens during contraction the lever is raised, and as it lengthens with diastole it is depressed (Fig. 175).

In using the perfusion cannula in the above experiments, a satisfactory nutrient fluid is defibrinated blood diluted with twice its quantity of normal saline; or a solution of normal saline, to which small quantities of calcium and potassium salts have been added, will do almost equally well (Ringer's fluid).

The Innervation of the Heart.

The heart, like the rest of the vascular system, is influenced by nerves which pass between it and a centre in the medulla oblongata, but it also contains within itself the mechanism necessary for its rhythmical action. This is readily demonstrated in the case of the frog's heart, which will continue beating for a variable length of time after entire separation from the body. The heart contains numerous ganglia, connected on the one hand with nerves reaching it from outside, and on the other with nerve fibres which pass to the muscular substance and the lining membrane. There thus fall to be considered both an *extrinsic* and *intrinsic* nerve mechanism, though the influence of the latter on the sequence of the events of the cardiac cycle, *i.e.*, upon the contraction of the heart and its rhythmical character, is disputed.

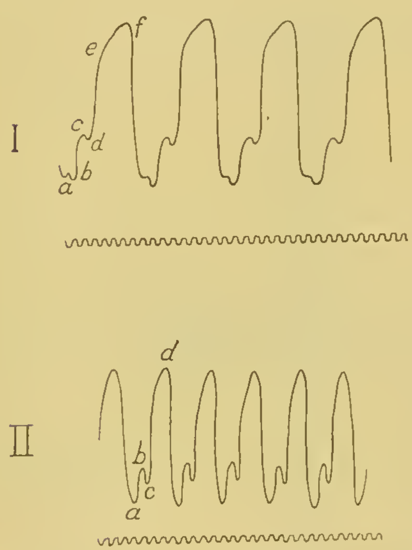


Fig. 175.—Tracings of Frog's Heart Contractions taken by suspension method.

I.—*a*, Sinus contraction; *b–c*, auricular contraction; *c–d*, relaxation of auricles; *d–e*, first part of ventricular contraction; *e–f*, last part of ventricular contraction, only shown in tracings from heart with full blood supply.
II.—*a–b*, Auricular systole; *c–d*, ventricular systole. Time, 4 per second.

The **intrinsic nerve mechanism.**—The arrangement of the ganglia in the frog's heart is more distinctive than in the mammal. The frog's heart differs also in some important ways in general construction from the mammalian, and these may be referred to shortly here. In the first place the ventricular wall, instead of being a solid mass of muscular substance, is broken up into a sponge-work of muscular trabeculæ, the meshes of which

communicate with the ventricular cavity. The columnæ carneæ and musculi papillares remain in the mammal as representatives of this condition. Posteriorly the sinus venosus receives the venous blood from the single inferior and two superior venæ cavæ, and from thence the blood passes into the right auricle. The left auricle receives the oxygenated blood from the lungs, and is completely separated by the auricular septum from the right auricle. Both auricles open into the single ventricle, from which the blood is sent into the bulbus arteriosus of the aorta and thence to the lungs and body. Owing to the sponge-like character of its wall, the left ventricle becomes deeply coloured when it is dilated and filled with blood during its diastole, and pales again when the blood is ejected during the systole.

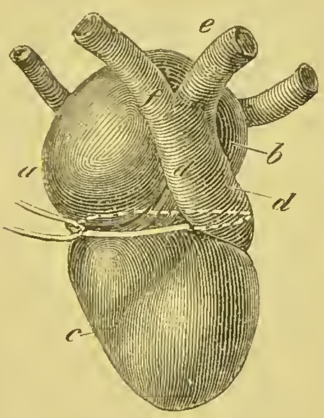


Fig. 176.—View of Frog's Heart from the Front.

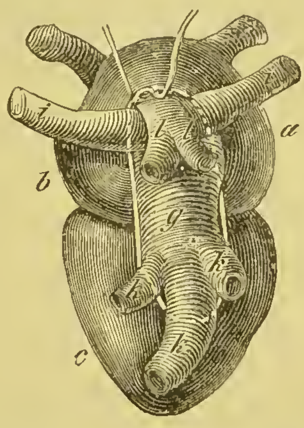


Fig. 177.—View of Frog's Heart from Behind.

k, Vena cava inferior; *g*, sinus venosus; *i*, venæ cavæ superiores; *a*, right auricle; *b*, left auricle; *c*, ventricle; *l*, pulmonary vein; *d*, truncus or bulbus arteriosus; *e*, ductus carotidus, ductus aorticus, and ductus pulmo-cutaneous.

The systole of the heart as a whole commences in the sinus venosus and spreads to the auricles and thence to the ventricle, the bulbus arteriosus being the last part of the heart to contract. With regard to the ganglia, a group—*Remak's ganglion*—which receives the two vago-sympathetic nerves is found on the sinus venosus, at the point where it joins the right auricle, and another, a double group—*Bidder's ganglia*—occurs at the junction of the auricle with the ventricle. A third group—Von Bezold's ganglion—is scattered over the inter-auricular septum, and hence these are sometimes known as the *septal* ganglion cells. From these ganglia, fibres pass to the walls of the sinus, the two auricles and inter-auricular septum, and to the ventricular wall, becoming less

numerous towards the apex. The nerve cells are unipolar for the most part, the single process dividing at a short distance from the cell; or the cell may be bipolar and pyriform, the one process winding round the other before it leaves it to pass in the opposite direction.

Generally speaking, though the nerve cells can thus be located in certain groups, they are distributed on the principle of being more numerous at the venous end of the heart and of disappearing as the arterial end is reached, till in the bulbus arteriosus they are absent altogether. In the lower vertebrates it is usual to find a collection of ganglionic cells at the junction of the sinus and auricles—that is to say, in the region of the circular muscular ring which marks the point of division between them; and another at the corresponding ring between the auricles and ventricles. The ganglia and nerves are situated superficially beneath the pericardium, and branches pass from them into the substance of the heart.

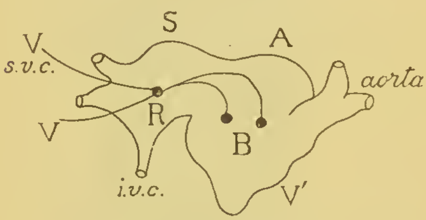


Fig. 178.—Scheme of Nerves of Frog's Heart.

V, Vagus; *V′*, Ventricle; *A*, auricle; *S*, sinus; *s.v.c.*, superior venæ cavæ; *i.v.c.*, inferior vena cava; *R*, Remak's ganglion; *B*, Bidder's ganglion.

In the frog the two vago-sympathetic nerves reach first Remak's ganglion (or the *sinus ganglion* as it is sometimes called), from which branches are distributed to the wall of the sinus and the auricles, and the two main nerves sinking deeply are continued along the inter-auricular septum, where they are connected with the septal ganglionic cells, until they reach Bidder's ganglia on the auriculo-ventricular ring, on the anterior side of the heart, and from these ganglia branches pass to the substance of the ventricle.

In the mammal the general plan already mentioned is followed, but the ganglia are not so definitely located as in the frog. The cardiac branches of the vagus and sympathetic nerves form deep and superficial plexuses about the root of the aorta, and the ganglia are most numerous about the roots of the great veins and in the auricles. They are also found in the auriculo-ventricular grooves and in the basal part of the ventricles.

The **origin of the heart beat.**—Though the heart of the frog and other cold-blooded animals will, under favourable conditions, continue to beat for hours, and it may be days, after removal from the body or general death of the animal, the mammalian heart

ceases to beat after a few minutes at most, and the frog's heart is thus the more convenient for the study of the rhythm. We have seen that in the frog's heart there is a distinct sequence of events, the sinus contracting first, then the auricles, and then the ventricle,* and its automatic pulsatile activity ceases in the reverse order, the ventricle being the first to become quiescent and the sinus the last. But even after the heart has ceased beating automatically, it still retains a certain measure of irritability for a varying length of time, and on being suitably stimulated by a prick of a needle or an electric shock, it may be induced to give one, two, or even more beats and with the usual sequence of events; though it must be borne in mind that occasionally only the part of the heart stimulated, be it sinus, auricles, or ventricle, will respond to the stimulus. As the irritability of the heart passes off, first the ventricle ceases to respond to stimuli, then the auricles, and then the sinus, the latter being thus the most irritable part. There is thus a descending series of irritability to external stimulus.

If the whole heart be bisected longitudinally, each half will continue to beat with a rhythm of its own—that is to say, not necessarily synchronously with the other half; and the halves of the bisected auricles, or of the entire ventricle alone, will also continue to pulsate. Further, if the auricular wall be divided into small pieces, each of these will also contract rhythmically, though feebly.

The question now arises—seeing that the heart possesses within itself the mechanism required for these rhythmical movements, which are essentially independent of influences acting upon it through the nerves from the medulla—Is this rhythmical energy inherent in the muscle fibres of the heart itself, or is it to be sought in the ganglia, which then may be considered to generate impulses which are transmitted by the nerve fibres passing from them to the cardiac muscle fibres, in the same way that the local ganglia control the movements of the wall of the stomach and intestines? In reply to this question two theories have originated, one of which, the earlier of the two, asserts the ganglionic, and the other, the later, the muscular origin of the rhythmical energy.

Theory of the ganglionic origin of the heart beat.—According to this theory the rhythm is the result of impulses starting in the nerve cells of the sinus ganglion, and transmitted from them to the walls of the sinus and to the ganglia of the auricular septum.

* Though this is the normal sequence of events, it must be noted that by the application of suitable stimuli at suitable moments the order of contraction may be reversed, the arterial end of the heart contracting first and the sinus last.

From these the impulses are transmitted to the walls of the auricles and to Bidder's ganglia, which in turn stimulate the ventricle to contraction. In support of this theory it was urged that if the apical portion of the ventricle, which contains no ganglia, be severed by a clean cut from the rest of the heart, it ceases to beat, the inference being that the cessation is due to its removal from ganglionic influence; while the rest of the heart, including sinus, auricles, and base of ventricle, goes on beating as before. And no spontaneous contraction will occur in the separated apex, though in response to a prick with a needle it may give an isolated beat. If the incision be carried instead through the auriculo-ventricular groove, the separated ventricle remains quiescent for a long time; when it begins to beat its rhythm is slower and the beats are irregular, and it will not continue so long as the part of the heart (sinus and auricles) which is left. If the incision be through the auricles so as to separate them and the rest of the heart from the sinus, the latter beats as before, but the auricles and ventricle will remain quiescent for a time, and then beat at a slower rate. There is thus a descending series of pulsatile power as well as of irritability, and what more natural than to associate this with the disposition of the ganglia in the relation of effect and cause? As we shall see immediately, however, there are several objections.

Theory of the muscular origin of the heart beat.—It is now generally supposed that the action of the heart is automatic, like that of the ciliated cell, and that it is therefore independent of nervous influence. Accordingly, the excitement is considered to rise in the muscle of the sinus and spread thence like a wave over the auricles and ventricle, being momentarily arrested or delayed in its course at the junction of the sinus with the auricles, and the auricles with the ventricle by the muscular rings which mark off these portions from each other. And there are many reasons for supposing this theory to be the correct one. In the first place, it is to be noted that the separated apex—*i.e.*, apical two-thirds, "heart apex"—of the frog's ventricle, if tied to a perfusion cannula and subjected to the passage through it of a nutritive fluid at a suitable pressure, will commence and continue to contract with a regular rhythm, and yet there are no ganglia in connection with it. Then in the embryo, the heart beats before any ganglia are developed in connection with it, and this alone is a strong argument, as it establishes the fact that, at one stage of life at least, the cardiac muscle cells are capable of acting rhythmically on their own initiative. Again, it has been found that removal of the septal nerves from the heart of the tortoise, and of the sinus ganglia and septal nerves from the heart of the frog, does not interfere

with the rhythmical beat, whereas if the walls of the auricles be cut or clamped so that the muscular continuity between them and the ventricle be interfered with, a marked effect on the ventricular beat, which may become reduced to one to every two or three of the auricles and sinus, results.

The effect of nicotine upon the heart is especially important as regards this question. Nicotine first stimulates and then paralyses the ganglion cells on the course of visceral nerve fibres. If the dose be increased the nerve fibres themselves become paralysed. Thus the vasomotor fibres passing upwards from the cord in the cervical sympathetic chain end in the cells of the superior ganglion, and from these proceed non-medullated fibres to the blood-vessels. If the cervical sympathetic be divided and its distal end stimulated, contraction of the blood-vessels of the ear (rabbit) results. If a drop of nicotine solution be now placed upon the ganglion and a little time allowed for the poison to act, stimulation at the same point as before, *i.e.*, on the proximal side of the ganglion, produces no result; but if the nerve on the distal side be stimulated, contraction of the blood-vessels of the ear takes place as before, showing that the block has taken place in the ganglion itself. If a drop of a weak solution of nicotine be placed upon the frog's heart, it is found that—(1) At first there is a slight slowing of the beat and a lessening of the height of the tracing, the effect soon passing off, and the heart continuing to beat normally. If the vagus* be now stimulated (2) no inhibition takes place, showing that the nicotine has caused a block at some point of the nerve mechanism; but a slight increase in the rapidity of the beats occurs, an augmentor effect due to the stimulation of the augmentor fibres in the vagus. If the electrodes be now applied to the septal nerves at the point where they leave the sinus ganglion, inhibition of the heart, as usual on stimulation of the vagus, is the result; (3) if the dose of nicotine be now increased, further and stronger stimulation of the sinus produces no effect in the way of inhibition, but the heart beats much more rapidly; (4) on withdrawing the stimulus the heart is at first quiescent but soon recovers its normal rhythm.

From this experiment we conclude that the nicotine produces a block in the ganglion cells, and that these are placed upon the

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* In the frog the vagus contains both inhibitory and augmentor fibres, the inhibitory being proper to the vagus itself and the augmentor being derived from the sympathetic. On stimulating the cardiac vagus in its course, the heart's beat is arrested in diastole. the action of the weaker augmentor fibres being thus overcome. (See "Extrinsic Innervation of Heart.")

inhibitory fibres of the vagus, and that the augmentor fibres pass by them. Further, that after the ganglion cells are paralysed, the non-medullated fibres passing from them to the muscular fibres still remain capable of stimulation, until upon the strength of the poison being increased they themselves become paralysed. As the heart continues to beat, and the augmentor fibres are not blocked, it is concluded that the cardiac movements are independent of motor ganglia, and that the augmentor fibres pass by the ganglion cells direct to the muscular tissue itself.

The action of atropine also supports the non-ganglionic theory of the heart beat. If it be injected into the circulation, or dropped upon the excised heart itself, the inhibitory influence of the vagus is abolished—that is to say, stimulation of the nerve does not produce inhibition of the heart, and it might be urged that this is due to paralysis of the inhibitory power of the ganglia. If now a strip of the auricle of another frog be taken it will continue to pulsate by itself, and if a very gentle interrupted current be passed through it, sufficiently strong to excite the fine terminations of the inhibitory apparatus in the heart wall, and not sufficiently strong to act as a direct stimulus to the muscular tissue itself, the strip will stop pulsating. But if a weak solution of atropine be applied, the pulsation will recommence in spite of the current. The atropine clearly acts by paralysing the fine nerve filaments or their terminations, or by affecting the muscular substance itself—that is to say, the same result is effected by stimulation of the vagus and of the terminal nerve filaments in the heart substance itself, and the intervention of any special ganglia with inhibitory power would thus seem to be unnecessary.

These four arguments—(1) That under suitable conditions the non-ganglionic ventricle will maintain a regular rhythm after separation from the rest of the heart; (2) that the fœtal heart beats rhythmically before ganglia are developed in connection with it; (3) that the removal of the septal nerves in the tortoise and frog does not interfere with the beat, while cutting or clamping of the heart substance, so that the muscular continuity of its parts is lessened, affects it markedly; and (4) that nicotine, which paralyses the ganglia, does not block the augmentor fibres which transmit their influence direct to the muscle—all lead to the conclusion that the beat does not depend on the action of motor ganglia. The ganglia may be trophic in their function and concerned with the nutrition of the heart.

Certain properties of the ventricular muscle.—As we have already seen in treating of the electrical changes in contracting

muscle (page 133), the wave of contraction in the heart travels from the base to the apex, and is accompanied with a lowering of the potential in the contracting part, giving rise to a diphasic variation. As we have also seen, if the apical two-thirds be separated from the base it remains quiescent until stimulated by a prick or an induction shock, when it gives a single beat and then resumes its quiescent state. But we have now to notice a striking difference between the response to stimuli of the heart and ordinary muscle. Whereas in the latter, within certain limits, the resulting contraction is proportional to the strength of the stimulus—a maximal stimulus producing a maximal contraction, and a minimal stimulus

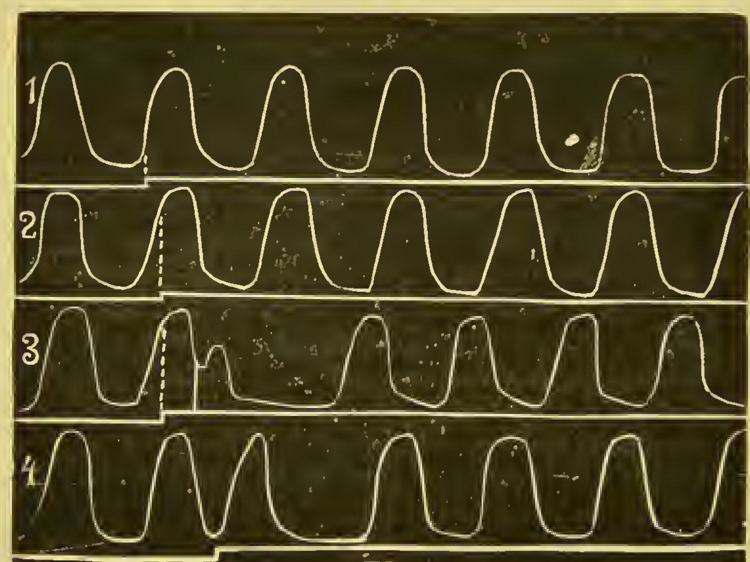

Fig. 179.—Refractory Period and Compensatory Pause.

A frog's heart was stimulated at a point marked by the nick in the horizontal lines. In 1 and 2 there is no result; in 3 and 4 an extra contraction, succeeded by a compensatory pause, is shown.

a minimal one—the case is different when we come to deal with the heart. If the stimulus be sufficient to provoke any contraction at all, it is a maximal, fully-developed one that results. In other words, with the heart it is *aut Cæsar aut nullus*—it is all or nothing. Moreover, the heart exhibits a much longer refractory period than ordinary muscle does. If in a beating heart the stimulus be thrown in before the contraction has attained its maximum height it produces no effect—the heart is "refractory"; if between the summit of one contraction and the commencement of a second, an extra contraction is the result. This, however, is

compensated for by a corresponding delay in the next beat, which falls, therefore, in the position which would have been occupied by the third beat if no extra contraction had been thrown in, the normal rhythm being thus restored. The refractory period is shorter for strong than for weak stimuli, and is diminished by heat, so that strong stimulation with the interrupted current at an increased temperature may result in a pseudo-tetanic condition, due to the increased rapidity of the beat, but owing to the lengthy refractory period there is no real fusing of the beats, and, moreover, these do not correspond with the vibrations of the interruptor. Needless to say, the ordinary heart beat is a single contraction and not a tetanus.

Though the isolated apex of the heart will not execute spontaneous rhythmic contractions, it may be induced to do so by chemical and mechanical stimuli. If the apex be placed in a slightly acid medium, its rhythmical contractions will continue till it dies, and we have already seen that the pressure of blood or nutritive fluid perfused through it will cause it to beat rhythmically. Moreover, a portion only of the ventricle will exhibit the same reaction to tension. A strip of the ventricle of the tortoise, if arranged to support a lever, and moistened with nutritive fluid, will contract rhythmically, and continue to do so owing to the stimulus of the stretching. The same rhythmical contractions may be noticed in stretched muscle in certain conditions of tension and in certain saline solutions, and the ureter of a dog will respond to distension with fluid in the same way.

These facts in connection with the muscle of the ventricle, in which there are no ganglia, and muscle in other situations, support the non-ganglionic theory of the origin of the heart beat in this way, that they show that muscle—cardiac, voluntary, and non-striped—is capable of rhythmical contraction in response to stimuli independently of the action of any ganglia; but the facts do not of themselves exclude the possibility of ganglionic influence upon the heart beat, or in any way explain the initiation of the cardiac contraction by the sinus. Apparently all we can say at present concerning this is that the wave of contraction does start there, and from the evidence at our disposal this seems to result from some greater inherent excitability of its muscular tissue.

When the apex of the ventricle is subjected to a series of induction shocks, the contraction is increased progressively, as in ordinary muscle for the first few stimuli, thus giving rise to a staircase tracing.

The **experiments of Stannius** have been the subject of much discussion. If the sinus venosus of the frog's heart be separated

from the auricle and ventricle by a fine ligature, the sinus will continue to beat while the rest of the heart remains quiescent. If a similar ligature be applied at the auriculo-ventricular junction, the ventricle will recommence to beat—feebly and at a slower rate—while the auricles remain quiescent. These results have been interpreted in different ways. According to those who hold the ganglionic theory of the heart's beat, the first ligature acts by stimulating the inhibitory mechanism, but this can scarcely be so as the standstill of the auricles and ventricle still takes place if the heart has previously been subjected to the action of atropine, which, as we have seen, paralyses the inhibitor fibres. And the effect of the second ligature would, according to the same theory, be due to the removal of the ventricle from the inhibitory influence. According to the supporters of the muscular origin of the excitation, the first ligature causes the arrest of the auricular and ventricular contraction by blocking an impulse passing from the sinus, and the second ligature stimulates the muscular fibre of the ventricle and so causes it to resume its beat for a time. But this should also cause the ordinary "apex-heart" to beat under similar circumstances, whereas it does not have that effect; nor can we on the same hypothesis (*i.e.*, of the ligature acting as a stimulus to the muscular fibres) explain the fact that neither the first nor second ligature so stimulated the muscular tissue of the auricles.

After the first ligature, when the auricles and ventricles are quiescent ("Stanniused heart"), if the auricle be stimulated by a pinprick, or an induction shock, it contracts and is followed by the ventricle; if the ventricle be first stimulated, ventricular contraction precedes that of the auricle. In either case only one contraction is the result of the stimulation. If the first ligature be so placed that the sinus ganglia are not completely cut off from the auricle, the auricles and ventricle will continue to beat, but at a slower rate. According to those who support the ganglionic theory, this is due to the ganglionic cells on the auricular side of the ligature initiating the muscular contraction; according to the opposite view the contraction arises in the automatically-acting muscular tissue on the auricular side of the ligature.

Gaskell's clamp is an instrument by which the auriculo-ventricular junction can be gradually compressed, the degree of compression being readily under control. The excised heart is held in the clamp, loosely at first, at the level of the auriculo-ventricular sulcus; a thread leading from the auricles to one lever and from the ventricle to another, the levers recording the contractions on a smoked drum. The clamp is at first sufficiently

open to allow the normal beat to be recorded. If it be now slightly screwed up the auricle and sinus continue beating as before, but the ventricle beats less frequently, perhaps at the rate of one of its own beats to two of the sinus and auricles. On further tightening the clamp the ventricular beat becomes reduced to one to three, or four, or five, of the auricular portion of the heart, and finally, on still further screwing up the clamp, it ceases to beat altogether. At first the impulse passing from the auricles to the ventricle is hindered by the commencing pressure of the clamp, but it can still pass through. It is,

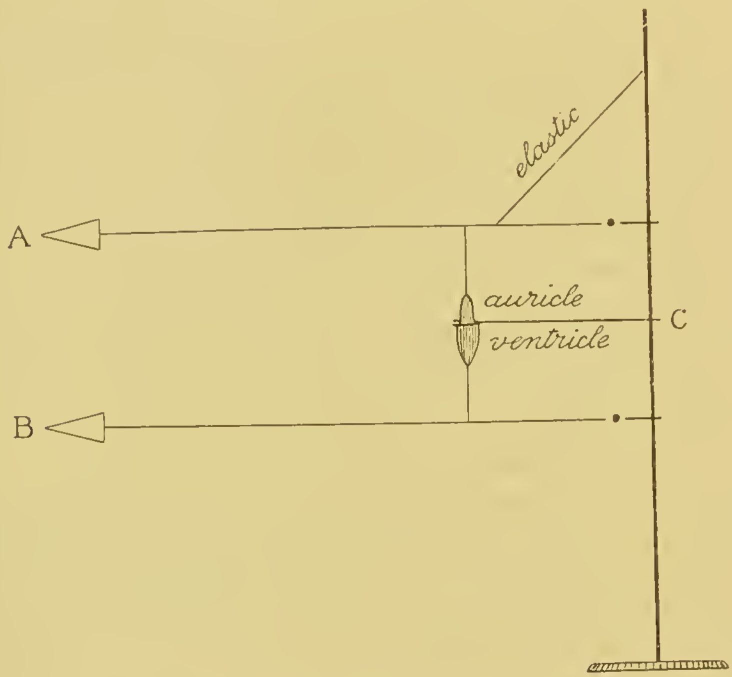

Fig. 180.—Principle of Gaskell's Clamp.

A, Lever connected with auricle; *B*, lever connected with ventricle; *C*, clamp,

however, enfeebled, and two or three or more stimuli are required to pass from the auricular side before the beat of the ventricle can be initiated (summation of stimuli). Finally the block becomes complete as the clamp is screwed up and no stimuli at all reach the ventricle. The same phenomena of slowing of the beat, succeeded by total stoppage, may be observed in the apical part of the ventricle when the clamp is placed mid-way between the apex and base of the ventricle instead of on the auriculo-ventricular sulcus.

The effects of heat upon a frog's heart held in Gaskell's clamp at the ariculo-ventricular junction are worthy of note. If the ventricle be heated the force of the beat is diminished and the frequency is not increased; but if the sinus and auricles be heated and not the ventricle, the frequency of the beat of the whole heart is increased. Of course this might equally well be due to the action of the increased temperature on either the ganglia of the sinus or the muscle wall, and it may be remembered in this connection that heat has a similar effect on the action of ciliated cells, where, of course, a nerve mechanism is not in question.

The **extrinsic nerves of the heart.**—Though the heart contains within itself the mechanism necessary to produce its rhythmical beat, it is subject to the influence of impressions reaching it from the medulla oblongata by the cardiac nerves, impressions which are *augmentor* and *inhibitory*. By augmentation is meant an increase in the strength or frequency, or both, of the heart beat; by inhibition a diminution of the strength or frequency, or both, even to the extent of complete arrest. We may first study the nerves of the frog's heart. Here the inhibitory fibres leave the medulla in the vagus nerve and proceed to the heart in the vago-sympathetic branches. The augmentor fibres leave the cord by a branch from the third nerve (anterior root) to the third sympathetic ganglion, whence they pass upwards along the sympathetic cord till they join the vagus, in which they pass to the heart along with the inhibitory fibres in the vago-sympathetic nerves. The vagus in the frog is thus augmento-inhibitory in its whole length, and to obtain the pure inhibitory effect it must be stimulated within the cranium before the sympathetic fibres reach it; to obtain the augmentor effect alone the sympathetic chain may be stimulated.

When the mixed nerve is stimulated with an interrupted current of moderate strength, the heart beat is usually arrested in diastole. On shutting off the current after a short interval, the heart commences to beat again, feebly at first, but with gradually increasing power. (A weaker current might have produced slowing and a diminution in the strength of the beats but not stoppage, *i.e.*, partial inhibition only.)

The effect of the stimulus is not immediately obtained, it will be observed in the tracing (Fig. 182), an entire beat succeeding the application, so that there is a distinct latent period. The beats succeeding the period of stimulation may show some augmentation until gradually the normal rhythm is resumed.

If the current be not shut off but continued, the heart remains quiescent for a few seconds and then slowly begins to beat again, the beats increasing in strength until the normal is reached. But often the beats show a distinct augmentation in frequency or strength, or both, for a time after the contractions have been restored, and this is due to the vagus in the frog containing both augmentor and inhibitory fibres. Whereas the latter are quickly raised to their maximum of stimulation, the reverse is the case

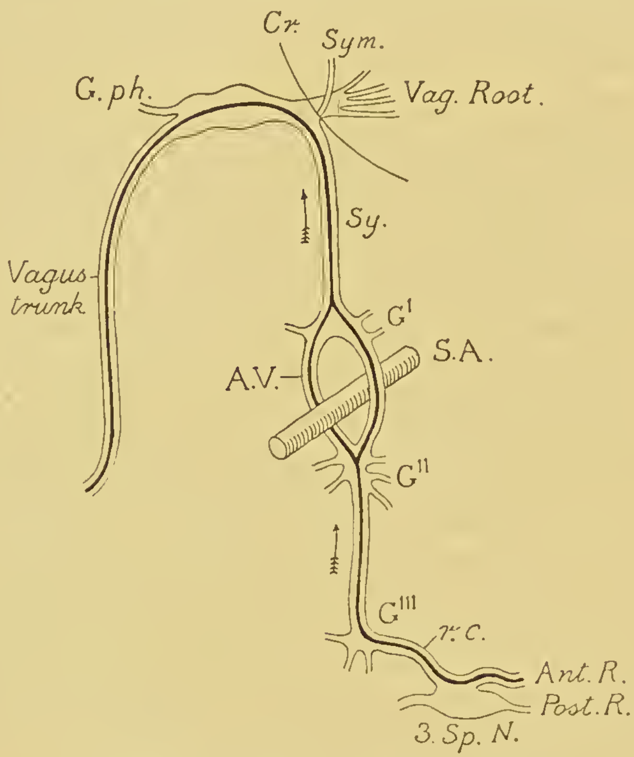

Fig. 181.—Cardiac Nerves of Frog.

Cr, Line of cranial wall; *G.ph*, glossopharyngeal nerve; *Sy*, cervical sympathetic; *S.A.*, subclavian artery; *G′*, first cervical ganglion; *G″*, second cervical ganglion; *G‴*, third cervical ganglion; *rc*, Ramus communicans; *3.Sp.N*, spinal nerve; *A.V.*, annulus Vieussens.

with the augmentor fibres, in which the effect of stimulation is slow to develop. Moreover, the inhibitory are much more quickly exhausted than the augmentor fibres. Hence it is that when the mixed nerve is subjected to the stimulation of the interrupted current, the first effect produced is that of inhibition, the augmentor effect only appearing when the inhibitory has worn itself out. As confirmatory of this explanation it may be said—

(1) That stimulation of the vagus in the skull, at a point before the sympathetic fibres join it, is succeeded by no secondary augmentation; (2) that stimulation of the sympathetic cord before it has joined the vagus gives rise to augmentation of the beats after a long latent period; and (3) that a weak stimulus applied to the vago-sympathetic nerve leads to little or no secondary augmentation, it being characteristic of the augmentor fibres that they require a strong stimulus to produce their effect, a weak stimulus being sufficient to excite the inhibitory fibres. But though the latent period of augmentation is greater than that of inhibition, it is not sufficient to account for the postponement of the augmentor effect till after the inhibition is over. The augmentation seems rather to be *delayed* till the inhibitory effect is exhausted; as if it could not develop and assert itself until the inhibitory influence were worn out.

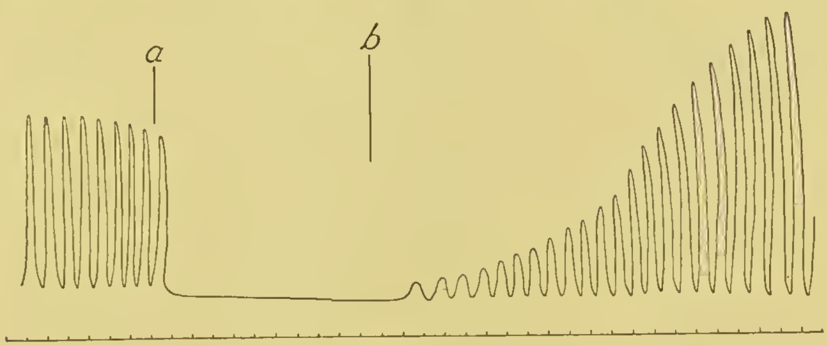

Fig. 182.—Stimulation of Vagus Nerve.

a, Point at which current was thrown in ; *b*, when it was shut off.

In the frog the auricle and ventricle are both affected alike, being inhibited or augmented in their action by stimulation of the nerves producing these effects. In mammals we shall see this is not the case.

We may now turn to the consideration of the cardiac nerves in the mammal. These are, as in the frog, augmentor and inhibitory. The *augmentor* fibres are derived from the sympathetic system and are connected with a centre in the medulla in the region of the vaso-motor centre. The fibres pass from the centre down the spinal cord, and in the rabbit leave it by the second and third dorsal nerves to pass to the first and second dorsal sympathetic ganglia, thence to the inferior cervical ganglion, whence they are continued as the *nervus accelerans* to the heart. The fibres are medullated at first, but lose their medullary sheaths in the

sympathetic ganglia, and are continued from this point as non-medullated fibres. If the nerves be divided as they leave the cord, or if the nervus accelerans itself be divided and the distal end stimulated, the contractions of the heart are augmented, *i.e.*, are increased in strength and usually in frequency, and this applies equally to the auricles and ventricles. But section alone of the nerve produces no effect, so that the augmentor influence is not exerted constantly. The *inhibitory* fibres of the heart are found in the inferior cardiac branch of the vagus. They arise from a cardio-inhibitory centre in the medulla, leave it by the roots of the spinal accessory nerve, and join the vagus immediately beyond the ganglion jugulare. In the dog the vagus and sympathetic branches are contained in a strong common sheath in which they run together, but not mixed as in the vago-sympathetic of the frog. In the rabbit the vagus and sympathetic are entirely separate in the neck.

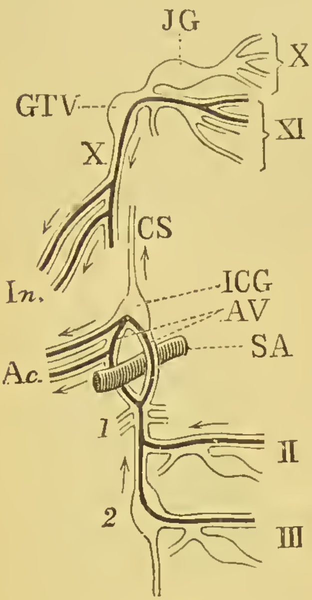

Fig. 183.—Diagram of Cardiac Nerves in the Dog.

II, III, Second and third dorsal nerves; SA., subclavian artery; AV, annulus of Vieussens; ICG. inferior cervical ganglion; CS, cervical sympathetic; 1, first thoracic ganglion of sympathetic; 2, second thoracic ganglion; Ac, accelerator or augmentor fibres passing off towards the heart; X, roots of vagus; XI, spinal accessory; JG, jugular ganglion; GTV, ganglion of vagus trunk; In, inhibitory fibres to heart.

If the inhibitory nerve be divided and its peripheral end stimulated, the heart is slowed and weakened, or if the stimulus be sufficiently strong, arrested in diastole, but, unlike the effect in the frog, the auricles and ventricles are unequally affected. The inhibitory fibres in mammals do not appear to have a direct effect upon the ventricles. The auricles are directly affected, their beat being weakened and retarded, and it may be altogether arrested as long as the current passes, though this arrest is not so easily brought about as in the frog. The ventricles are *slowed*, not because of any direct inhibitory influence, but because they are dependent on the auricles for their stimulus; but the strength of their contraction is not diminished. When the auricles are completely stopped, the ventricles follow suit for a time, but soon start beating again with an independent rhythm. Thus the inhibitory effect is more limited in its distribution than the augmentor, which, as we have just seen, affects the auricles and ventricles equally,

increasing the strength of their contraction and, as a rule, the frequency.

Certain drugs have a special effect on the cardio-inhibitory mechanism. *Atropine* paralyses the inhibitory nerve endings (page 192). *Nicotine* paralyses the ganglia only at first, so that stimulation of the sinus (which is virtually the same as stimulation of the fibres between the ganglia and the muscle) will cause the heart to stop beating. *Muscarine* causes the heart to be arrested in diastole, by stimulating the inhibitory fibrils between the ganglia and the muscle, or the endings in the muscle itself. If a heart be poisoned with nicotine, and muscarine be subsequently applied to it, the latter will yet produce its usual effect, as it is free to act on the nerve fibrils between the ganglia and muscular fibres. But a heart poisoned with atropine is immune to muscarine as the mechanism is already paralysed. On the other hand, a heart inhibited by muscarine can be recovered by atropine, which paralyses the parts which muscarine stimulates and so antagonises it. That these two drugs act upon the nerve fibrils and not on the muscular substance of the heart itself is shown by the fact that they have little or no effect on the hearts of young embryos.

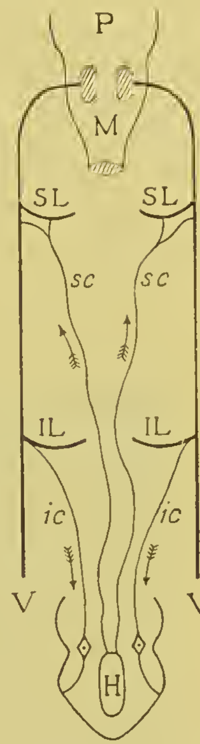

Fig. 184.—CARDIAC BRANCHES OF VAGUS IN RABBIT.

P, Pons; *M*, medulla; *V*, vagus; *SL*, superior laryngeal nerves; *IL*, inferior laryngeal nerves; *sc*, superior cardiac nerves; *ic*, inferior cardiac nerves; *H*, heart.

The cardio-inhibitory nerves are constantly in action (in this way contrasting with the augmentor), holding a rein, as it were, on the beat of the heart. Accordingly, if the vagus be divided on both sides in the dog, cat, or rabbit, the beat of the heart becomes quickened.

Reflex inhibition through the vagus.—The heart may, however, be inhibited reflexly, as well as directly, thus—(1) Stimulation of some sensory nerves can inhibit the heart's action. An instance of this is afforded by the inhibition of the heart following a violent blow on the epigastrium. Here the afferent nerve is the abdominal sympathetic, which conveys the impulse to the centre in the medulla, whence it is transmitted by the vagi to the heart. The superior cardiac branch of the vagus is another sensory

nerve, stimulation of the central end of which produces a sensation of pain in the region of the heart, inhibition of the heart's action, and a fall of blood-pressure, and to this last phenomenon especially we shall refer more fully later. It is the sensory nerve of the heart, and conveys impulses to the medulla which are transmitted through the cardio-inhibitory centre down the vagi to the heart. Other sensory nerves also may convey impressions to the medulla which inhibit the heart. If the foot of a frog be crushed the heart may be stopped, but this is not invariably the case. If the central end of the divided sciatic nerve be stimulated, the first effect is simple augmentation, which is sometimes succeeded by a sudden reflex inhibition through the vagus; (2) stimulation of the central cut end of one vagus may produce reflex inhibition, the impulse passing down the other; (3) emotion may stimulate the inhibitory centre, and so inhibit the heart; (4) a venous state of the blood in the rabbit has a similar effect — if the nostrils be covered with the hand for a few seconds, so that respiration is stopped and the blood ceases to be oxygenated, the heart rate becomes markedly slower; (5) increased arterial pressure stimulates the centre, and the higher the pressure the more slowly does the heart beat. This law, however, only holds if the vagi be intact. If the blood-pressure be raised, *e.g.*, by clamping the aorta, the vagi being previously divided, no such inverse relation ensues.

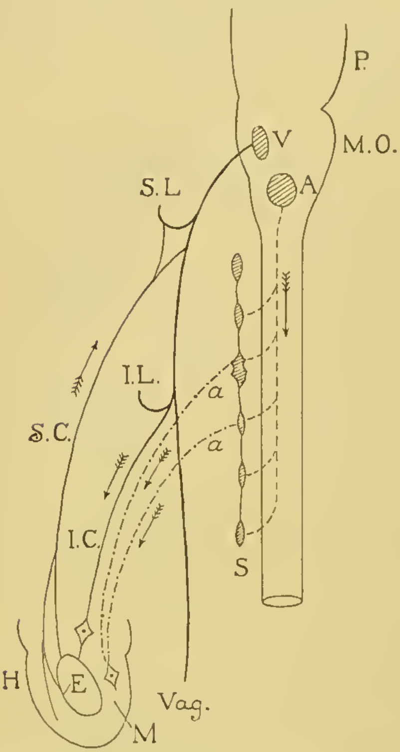

Fig. 185.—Scheme of Accelerator, Inhibitory, and Sensory Nerves of the Heart.

P, Pons; *MO*, medulla oblongata; *V*, inhibitory centre for heart; *A*, accelerator centre for heart; *Vag*, vagus; *SL*, superior laryngeal nerve; *IL*, inferior laryngeal nerve; *SC*, superior cardiac nerve; *IC*, inferior cardiac nerve; *H*, heart; *E*, endocardium; *M*, muscular subcutaneous; *S*, cervical sympathetic; *aa*, accelerator fibres.

Nature of augmentor and inhibitory action.—As we have already seen, there is reason to suppose that the ganglia of the heart

do not act as local centres for the production of the heart beat or the regulation of its rate, but that the heart muscle itself possesses the power of initiating its contractions; and similarly that there is no evidence that the ganglia, though situated on the inhibitory nerves, have any power of determining the character of the impulses transmitted to the heart by the vagi, or of themselves originating inhibitory impulses. With regard to the nature of the inhibitory and augmentor influences transmitted to the cardiac muscle by the vagus and sympathetic nerves, this at present is matter of doubt. According to some, the influence of the vagus is *anabolic*—that is, trophic or constructive, leading to a diminution of the destructive katabolic changes underlying or subtending contraction; while that of the augmentor fibres is *katabolic* or destructive, facilitating these changes underlying contraction, and hence leads to increased work. And it agrees well with this theory that the action of the inhibitory influence should be restorative, leaving increased capacity for work when the stimulus is withdrawn, while that of the augmentor influence is the reverse and is succeeded by exhaustion.

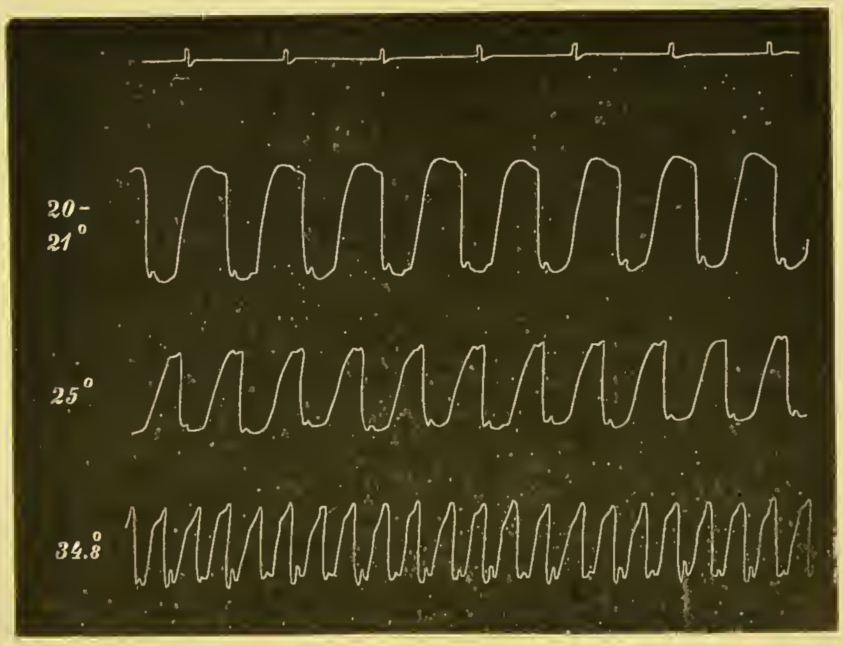

Fig. 186.—Effect of Temperature on the Beat of the Isolated Heart of a Cat.

Certain other conditions affecting cardiac action.—1. *Temperature.*—Heat accelerates the heart till a certain point is reached, when the beats become slower and finally the heart

becomes quiescent, with the ventricles contracted in a condition of *heat rigor*. Up to 20°C. the size, extent, and rapidity of the contractions increase, the duration of one of them at this temperature being only $\frac{1}{10}$th of what it is at 5°C. Cold has an opposite effect, the heart beating more slowly than usual, and in the case of the frog ceasing to beat at from 4° to 0°C. The effect of heat and cold may be studied with the frog manometer, the fluid in which the heart is placed being at any temperature required; or, more simply, the excised heart, with a light lever resting on the ventricle, may be placed on a slide and heat applied to the under surface with the flame of a spirit lamp, or cold by means of small pieces of ice resting against the heart.

2. *Blood-pressure.*—The stimulating effect on the cardio-inhibitory centre of an increase of arterial pressure has already been mentioned. Rapid return of the venous blood to the right side of the heart causes acceleration of the heart beat by stimulating the lining membrane, and in this way muscular exertion is accompanied with a more rapid heart beat.

3. *Muscular effort* accelerates the heart's action by hastening the return of venous blood to the right side of the heart. This it does by compression of the veins, in which the valves admit of the blood flowing in one direction only. At the same time the peripheral resistance is increased, and if the exertion be carried too far, the heart, struggling against this and distended with the blood returned by the venæ cavæ, may come to a standstill, unable to expel its contents.

4. *The posture of the body.*—The heart beats more quickly in the erect position of the body; more slowly in the recumbent.

5. *Period of life and sex.*—The heart of an adult male beats on an average 72 times per minute, of the adult female 80 times, but in each case it may vary within considerable limits, sinking as low in some cases as 55 and in others rising to 100. At the end of fœtal life the pulse rate is given as 144–133, from ten to fifteen years 91–76, from twenty to twenty-five years 73–69, at which it remains till sixty years, a slight increase in the rate occurring in old age.

6. *Period of the day.*—During a period of fasting and resting the pulse rate decreases somewhat during the day up to 2 p.m., and then slightly increases again. During sleep it may fall as low as 50 beats per minute. Cold food does not alter the rate, but hot meals may increase it by ten.

7. *The state of the nervous system.*—The inhibitory centre may be stimulated, as we have seen, by emotion, such as fright, resulting in cessation of the heart beats, and syncope or fainting.

The brain, including the cardiac centre in the medulla, is thus deprived of blood, and the first requisite for recovery is to place the patient in a recumbent position, with the head entirely unsupported with pillows, and, if anything, at a lower level than the rest of the body. The strain on the heart of supporting a vertical column of blood is thus removed and the flow to the head rendered easier. A dash of cold water in the face stimulates the fifth nerve and thus induces a deep inspiration. Smelling salts, such as those of ammonia, stimulate the nasal branch of the fifth nerve and excite cardiac and respiratory action. Brandy poured down the throat may stimulate the cardiac centre, first reflexly from the gastric mucosa and then directly through the blood-stream. A hot sponge over the precordial region will sometimes induce reflex contraction of the heart. Lastly, ether, which is a very rapidly-diffusible stimulant, may be injected hypodermically.

8. *Chemical agents.* — Some of these have been already studied, and little but the names of others can be here mentioned. Digitalis increases the ventricular contraction, so that the heart empties itself as completely as possible, and slows the rate. Alcohol increases the frequency and force of the heart beats. Ether and chloroform first suspend consciousness, then the action of the respiratory centre, and then that of the cardiac centre. Chloroform causes respiratory and cardiac failure sooner than ether does. If two rabbits be anæsthetised by supplying the one with ether to inhale and the other with chloroform, it will be found that the chloroformed one dies first; and the effect upon the heart can be observed by sticking a needle bearing a straw and flag into each heart through the chest wall. As the hearts contract and displace the needles, the flags move, and the action of the two hearts can be compared, when it will be observed that the flag of the chloroformed rabbit ceases to move first.

CHAPTER VI.

BLOOD-VESSELS AND THE MOVEMENTS OF BLOOD IN THEM.

The Structure of Arteries, Capillaries and Veins.

Structure of the arteries.—A medium-sized artery, such as the radial, has three coats—internal, middle and external. The *intima* or *internal* coat is composed of a lining of flattened epithelial cells (nucleated and fusiform in outline, placed with their own long axis in that of the vessels they line, and united

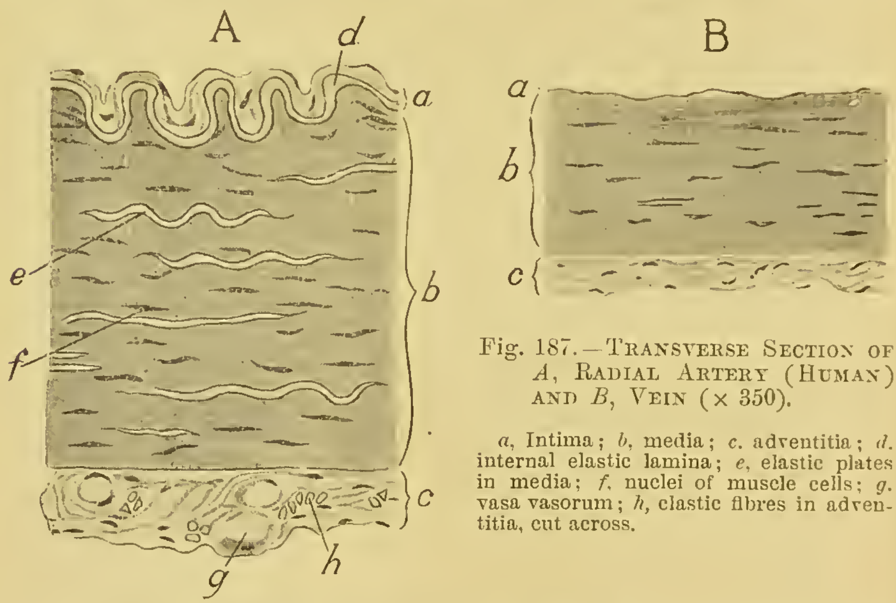

Fig. 187.—Transverse Section of *A*, Radial Artery (Human) and *B*, Vein (× 350).

a, Intima; *b*, media; *c*, adventitia; *d*, internal elastic lamina; *e*, elastic plates in media; *f*, nuclei of muscle cells; *g*, vasa vasorum; *h*, elastic fibres in adventitia, cut across.

to each other by cement substance) resting on a layer of subendothelial connective tissue, bounded by the internal elastic lamina. The subendothelial tissue consists of branched cells in a delicately-fibrillated matrix of white fibres, and the internal elastic lamina is a fenestrated elastic membrane, which is thrown into longitudinal folds when the artery is contracted after death. In the smaller arteries and arterioles the subendothelial connective

tissue disappears and the epithelial cells rest directly on the internal elastic lamina. The *media* or *middle* coat consists for the most part of concentrically-arranged non-striped muscle fibres, with the addition of fenestrated elastic plates interspersed among them, and a small quantity of areolar tissue. The media forms the main part of the artery, being the thickest of the three coats, and from its constitution is both contractile and elastic. The *outer* coat or *adventitia* consists of elastic fibres or fenestrated membranes supported by ordinary white connective tissue. It is the toughest and most resistant part of the artery, but from the absence of muscular fibres it is not contractile. Blood-vessels

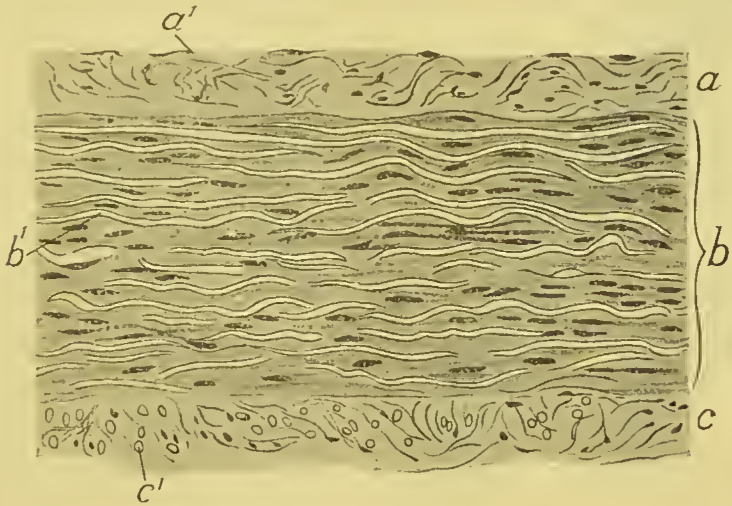

Fig. 188.—Transverse Section of Aorta of Dog.

a, Intima; *a′*, epithelium; *b*. media; *b′*, elastic plates; *c*, adventitia; *c′*, elastic fibres cut transversely.

(vasa vasorum) for the nourishment of the arterial wall itself are found for the most part in the outer coat, but branches penetrate for some distance into the media. The intima is extra-vascular. Nerves of the non-medullated variety pass through the outer to the middle coat, where they end in connection with the muscular fibres. The external coat must not be confounded with the sheath in which the whole artery lies. This sheath consists merely of a condensation of the connective tissue surrounding the vessel, that is of ordinary areolar tissue, so that it is less elastic than the artery it contains.

As we pass upwards or downwards along such an artery, certain changes in the proportion of the elements of which it is composed may be observed to take place. Generally speaking, the larger the

vessel the more the elastic element is in evidence, and the smaller it is the more distinct is the muscular contractile element; elasticity being the most conspicuous feature of the larger arteries, and contractility of the smaller. In the aorta, for example, the middle coat possesses a relatively larger number of elastic plates, together with a considerable amount of ordinary white connective tissue, and its elasticity is much more marked than its contractility, which is decidedly small; but in one of the small arteries of the hand or foot, the media forming nearly the whole thickness of the wall is almost entirely muscular, and its elasticity, though considerable, is entirely masked by its contractile properties.

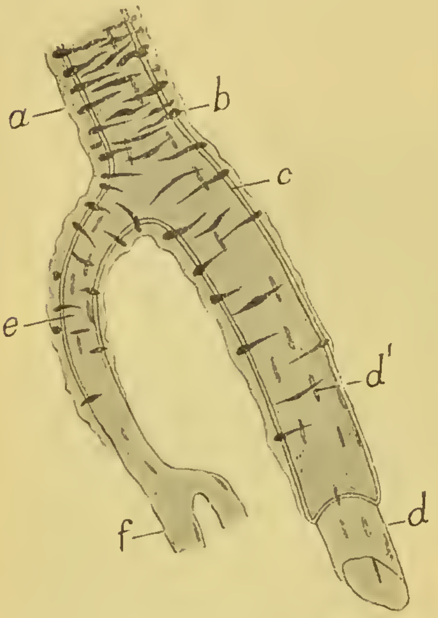

Fig. 189.—Small Artery in Membrane (Pia Mater of Sheep).

a, Adventitia; *b*, muscle cell of media; *c*, internal elastic lamina of intima; *d*, epithelium; *d'*, nuclei of epithelium; *e*, smaller artery; *f*, capillary.

Structure of the capillaries.—If the pia mater of a sheep or other animal be examined under the microscope it is found to be a very vascular membrane, and the characters of the smallest arteries and veins and capillaries may readily be observed in it. The minute arteries possess, as before, an endothelial lining of fusiform cells, which here rest directly on a delicate elastic membrane, the representative of the internal elastic lamina. Outside this a thin layer of transversely placed muscle fibres may be seen — the remains of the muscular layer— and beyond this a very delicate connective tissue sheath, representing the adventitia. As the artery reaches the capillary area, the muscular layer thins out, the cells becoming discontinuous and finally disappearing, and the adventitia becomes indistinguishable from the connective tissue in which the vessel lies. The capillary itself consists merely of the endothelial lining, and thus forms a tubular anastomosing passage lined with epithelium in the connective tissue. The latter is bathed with lymph, and thus between the blood-stream in the capillary and the lymph outside it, nothing but a thin transparent epithelial membrane intervenes, which

permits of a ready passage of fluid or gaseous substance in either direction.

As the capillary is followed on into the veins the elements of the arterial wall, speaking generally, begin to reappear. The structure of the smallest veins or venules in the capillary region differs from that of the arteries to which they correspond, in that the lumen is wider, the walls thinner, and the cells of the epithelial lining are broader and shorter.

Structure of the veins.—The veins resemble the arteries, except in the points of difference just given and the fact that they contain valves. The *intima* consists of a layer of epithelial cells, broader and shorter than those of the artery, resting on a subendothelial tissue in which the elastic element is in the form of a network of fibres rather than a distinct fenestrated membrane, so that the striking internal elastic lamina of the artery is conspicuous by its absence. The *media* consists of an admixture of connective tissue of white and elastic elements with muscular fibres, the latter forming a kind of meshwork, for the most part disposed transversely. The *adventitia* shows a basis of white fibres with elastic fibres intermingled. Sometimes muscular fibres are present, when they are placed longitudinally. As in the arteries, vasa vasorum run in the adventitia and penetrate the media. In some of the large veins the middle and outer coats are more or less commingled, and the muscular fibres run chiefly longitudinally or obliquely, and may be present in only small quantity, or in considerable number, as in the portal vein. The veins, in fact, vary a good deal in their structure in different situations, but generally speaking, they have not the elasticity and contractile power of the arteries, in accordance with the more passive function they have to serve.

Most veins have valves, the exceptions being found in those of the viscera, the central nervous system, and the bones, which are without them. In structure the valves are virtually reduplications of the lining membrane directed towards the heart. They are most numerous in the veins of the extremities, and may consist of a single semilunar fold in the smaller veins, or of one or two or more in the larger. They are absent in the situations mentioned, and in veins of less than a line in diameter.

The Pulse.

The **pulse** is the expansion of the arteries which occurs at every contraction of the heart. The expansion is temporary, and, as we have seen, this recurring temporary increase in the contents

of the vessels occurs only in the arterial system, disappearing in the capillaries and veins, in the constant mean pressure of which no oscillations occur. We have also seen that the disappearance of the pulse at the end of the arterial tree, where it becomes lost in the capillary region, is due to the elasticity of the arterial walls, which allows of their expanding to receive a greater quantity of blood than escapes from them during the systole of the heart, and to the contracted state of the arterioles or smallest arterial twigs, which enables the blood to be "heaped up" in the arterial system behind them. The pulse then corresponds to the intermittent outflow from a system of tubes which are elastic, but from which the outlet is not sufficiently restricted to allow of the heaping up in them of sufficient fluid to maintain the outflow during the intervals between the contractions of the pump.

This sudden expansion of the vessels, known as the pulse, is due to the blood thrown into the arterial system at every systole of the heart, and is followed by an elastic recoil of their walls, which takes its part in driving the blood onwards, the kinetic energy of the heart having thus in part been converted to the potential energy of the vessel wall. But the elasticity of the arteries is of service in other ways than those of enabling them to accommodate themselves to varying quantities of blood thrown into them, and of permitting a continuous stream in the capillaries and veins. The friction of the blood in passing through is very much reduced by their elasticity, and the mechanical shock which would replace the pulse if the tubes were rigid is avoided.

If a lever be placed upon an artery, such as the radial, it rises with the distension of the vessel and falls again with its recoil, and a record of its movement may be taken on a rapidly-moving surface, which is called a *pulse curve* or *tracing*. The curve is, however, merely the record of the movement, up or down, of the arterial wall on which the lever rests, and must not be regarded as a representation of the pulse wave which causes it in its passage along the vessel. In such a curve we see that the upstroke of the lever corresponding to the systole of the heart is sudden, uninterrupted, and nearly upright, whereas the downstroke, due to the elastic recoil of the artery, which takes longer to develop, is more gradual and has certain irregularities upon it, the significance of which we shall see immediately (Fig. 192).

The "pulse wave" is a wave of expansion passing along the artery when the ventricle has contracted. A certain volume of blood is thrown into the first part of the vessel springing from the heart, which, being thus dilated, and at a higher tension than the succeeding part, contracts and forces some of its contents into it,

so that this second part is itself dilated and at a greater tension than the succeeding, so that it contracts in like manner in its turn; and this is continued along the arterial tube to its termination. By adjusting two levers on a vessel, the one nearer to the heart and the other near the periphery, and arranging them to write, the one immediately beneath the other, on a moving surface, two pulse tracings are obtained, the curve of the one commencing at an appreciably later period than that of the other. If the length of the vessel between the two levers be ascertained, and the time between the commencements of the upstrokes of the two curves, we get the *velocity of the pulse wave* by dividing the distance by the time. Thus, if the distance travelled be one metre, and the time be one-sixth of a second, the rate of the pulse wave will be six metres per second. It has been variously estimated at from ten to five metres per second. The rate of the pulse wave is largely dependent on the elasticity of the vessels, the greater the elasticity the slower will be the wave, while in a perfectly rigid tube it would be converted into a very rapid shock, occurring almost simultaneously throughout the vessel. But in two tracings taken, as we have described, there are other points to note besides the time relations of the curves. The curves themselves differ. In the one nearest to the heart the upstroke and downstroke are both more sudden than in the other, and, moreover, the height of the curve is greater. And if we were to adjust a number of levers, instead of two only, we should find that they afforded tracings showing the progressive flattening out of the curve as the heart was receded from and the region of the obliteration of the pulse approached; and for this reason, that as the heart is further and further receded from along the arterial tree, the elasticity of the vessel walls progressively brings the oscillations above and below the mean pressure, caused by the systole of the heart, more and more under control, until when the capillary area is reached they have disappeared altogether.

The *length of the pulse wave* is readily estimated when its velocity is known. If the velocity be six metres per second, and we ascertain from the pulse tracing that the wave has lasted during the whole systole of the heart (for the downstroke is succeeded immediately by the upstroke of the next curve), then it lasts eight-tenths of a second, and at a rate of six metres per second it will be nearly five metres in length. This is more than is required to cover the distance from the heart to the capillaries of the toes—a distance of under two metres.

The rate of the pulse wave is much more rapid than that of the blood-stream itself, and the two must not be confused

with each other. "The pulse-wave travels over the moving blood somewhat as a rapidly moving natural wave travels along a sluggishly flowing river" (Foster). The current of the blood is only one-half metre per second, even in the large arteries, as contrasted with the ten to five metres per second of the pulse wave.

We have seen that the downstroke of the pulse curve was broken by certain irregularities, and we have now to consider more particularly their significance; but a few words may first be said as to the methods by which such tracings are more usually taken. A somewhat similar curve to that figured on page 213 may be obtained without the intervention of any lever, by allowing an artery cut transversely to spirt against a rapidly-moving surface. Such was Landois' method, and such a tracing is called a "hæmatograph." This is obviously, however, not a very available

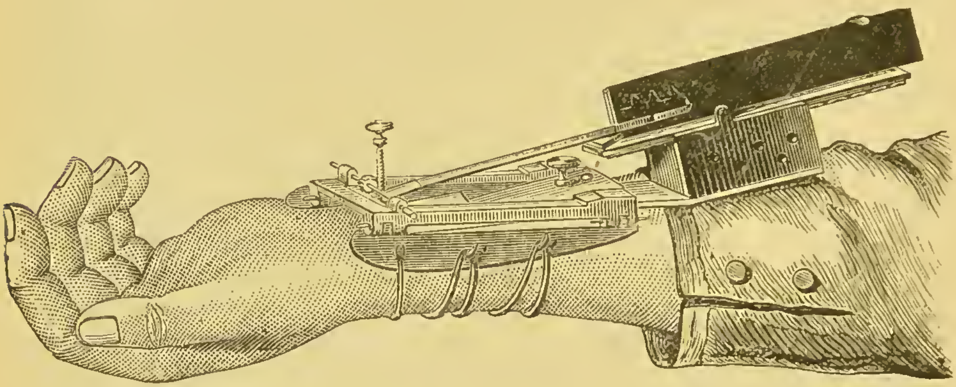

Fig. 190.—Marey's Sphygmograph.

or convenient method, and the principle of the lever is the one commonly adopted. The pulse curve is usually taken by means of a sphygmograph, as it is called, the two in most common use being Dudgeon's and Marey's. In both the principle is the same, that of a spring pressing upon the artery, and by means of a system of levers writing on a moving smoked surface. The spring requires to be specially adjusted; its pressure on the blood-vessel wall must be neither more nor less than is required to bring out the various features of the curves. If the pressure be too slight, the rise of the curve is too small, and over pressure produces a similar result, as the artery is unable to sufficiently raise the spring. The two instruments mentioned are shown in the accompanying figures, and the details of their mechanism need not detain us here. Each can be readily adjusted

by means of a milled head, so that the spring exerts the right pressure on the vessel; the smoked paper is run by a clock-work

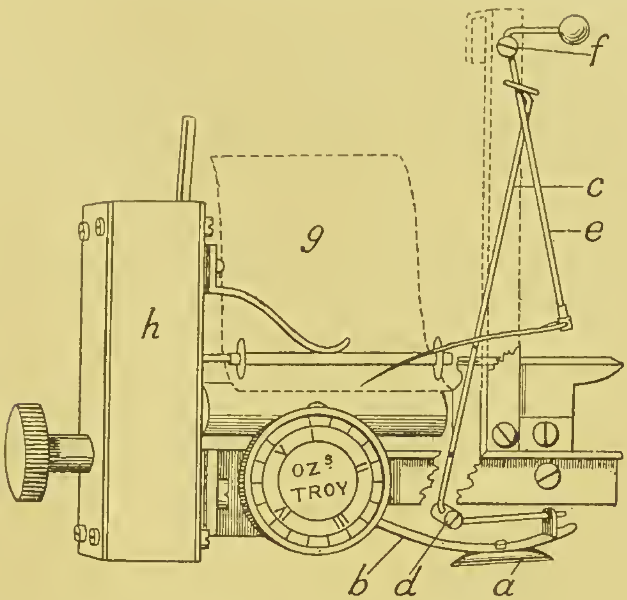

Fig. 191.—Diagram of Dudgeon's Sphygmograph.

a, Metal plate which is pressed on the artery by the spring *b*, and which by its rise and fall moves a system of levers, *c*, *d*, *e*, *f*; to the free end of *e* is attached a light steel marker, the pointed extremity of which rests on a strip of smoked paper, *g*. The paper travels between two small wheels and a roller which is set in motion by a clock-work arrangement in the box *h*. The graduated milled head rotates a camm, by which the pressure of the spring *b* on the artery is regulated.

arrangement; the whole instrument being fastened to the wrist (the usual site) by tapes. In a pulse tracing obtained in this way some such curve as is shown in Fig. 192 is found. Each cycle of the heart is represented by a *primary* curve, upon the descending limb of which *secondary waves* are to to be seen. Of these, three are shown in the figure, of which by far the most important is the middle one, *d*, which is present in all normal tracings and is called the *dicrotic wave.* That immediately preceding it, *c*, is termed the *predicrotic wave*, and the dip between the two the *dicrotic*

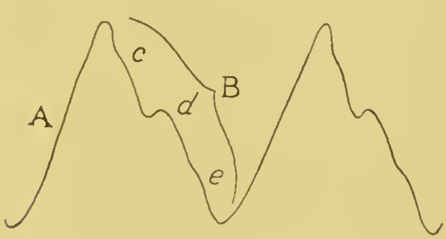

Fig. 192.—Diagram of Pulse Tracing.

A, Up stroke; *B*, down stroke; *c*, predicrotic wave; *d*, dicrotic wave; *e*, postdicrotic wave.

notch. The wave following the dicrotic, marked *e*, is the *post-dicrotic wave*, and of these there may be more than one. As to the significance of these waves—*catacrotic* as they are called, for they occur on the descending limb of the curve—discussion has raged freely. That the dicrotic is not a wave reflected from the periphery back to the heart, *i.e.*, a centripetal wave, is shown by the fact that at whatever distance from the heart the tracing is taken the dicrotic wave is found at the same distance from the primary rise.

The following seems to be the more generally accepted view :—The dicrotic wave, which, as we have said, is the most constant and most important, is associated in some way with the valves of the aorta. If tracings be taken simultaneously of the pulse, the aortic and intra-ventricular pressures, and the apex-beat, it is found that the predicrotic wave is situated in the systolic part of the curve, which terminates at the commencement of the dicrotic wave. The dicrotic wave, in other words, corresponds fairly accurately with the closing and stretching of the aortic valves, and is attributable to the rebound of blood from them, which, in conjunction with the elasticity of the aortic wall (in virtue of which it tends to dilate again after its first contraction upon the blood thrown into it at the ventricular systole) leads to a second dilatation of the vessel, and thus (for these effects are transmitted through the whole of the arterial system) causes the lever of the artery to be again thrown up and to record the dicrotic wave.

The postdicrotic wave or waves are regarded as mere oscillations of the elastic arterial wall.

Of the predicrotic wave nothing of any certainty is known. By some it is classed with the postdicrotic, as an oscillation wave; by others it has been attributed to the inertia of the sphygmograph, the lever being carried too far by the first impact of the blood from the ventricle, falling again on the still tense artery, and then springing up again to describe the predicrotic wave.

The form of the curve varies with the condition of the heart (*i.e.*, the rapidity and force of contraction of the pump) and the vessel wall. If the heart is beating with ordinary vigour, and the arterial wall is lax, the tension being low, the ascent of the primary wave is sudden, high, and pointed at the apex, the descent being proportionally rapid and the dicrotic wave well marked. These features are readily understood on physical grounds. The blood thrown into the aorta with lax walls causes these to expand quickly, and they fall equally quickly when the systole is over; in the same way the rebound of the blood from the aortic valve

will distend the walls of a poorly filled vessel more than it would those of one well filled, in which the tension is already high. The predicrotic wave is insignificant or absent, and if it be regarded as due to the inertia of the lever, this is explained by the comparative laxity of the vessel wall on which the lever falls. If due to the oscillation of the arterial wall, its absence would be accounted for by laxness of the membrane. On the other hand, if the arterial wall be contracted and the tension high, the blood does not so rapidly leave the heart, as it has to make its way against the pressure in the already tense aorta; and the rise is not so sudden nor so high, the curve being more rounded on the top. The dicrotic wave is not so well marked, as the rebound from the aortic valves has not the same marked effect on the tense walls of the well-filled aorta as it had on the walls of the lax vessel. But the predicrotic wave is distinct, either because the lever falling upon the tenser wall rebounds proportionately or because oscillations occur more readily in a tense membrane.

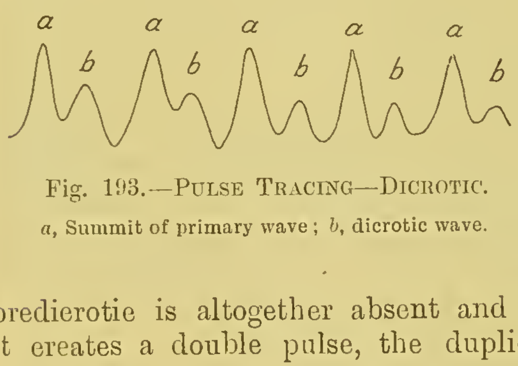

Fig. 193.—Pulse Tracing—Dicrotic.

a, Summit of primary wave; *b*, dicrotic wave.

Thus, in the hard pulse, the dicrotic wave is small and the predicrotic distinct; in the soft pulse the predicrotic is insignificant or absent, and the dicrotic is conspicuous. If the pulse be very soft, and the heart be beating quickly and strongly, as in fever, the predicrotic is altogether absent and the dicrotic so marked that it creates a double pulse, the duplicate character of which can be readily distinguished at the wrist. Such a tracing is called "dicrotic." On the other hand, in old people, in whom the arteries are often rigid, the arterial tension high, and the heart hypertrophied, the dicrotic wave is almost absent. In those diseases, too, in which the peripheral resistance is high, what is termed an "anacrotic" pulse sometimes occurs. In the curve from this pulse a secondary wave is found on the primary upstroke, apparently due to some

Fig. 194.—Anacrotic Pulse Tracing.

a, Secondary wave in up-stroke; *b*, summit of up-stroke; *c*, predicrotic wave.

intermittenee in the foree of the ventricular contraction, a relapse oeeurring after its start, followed by renewed contraction till the maximum is reaehed. It is found when the ventricle expels its eontents slowly against resistanee, as when the arteries are rigid, the mitral valve stenosed, and the heart hypertrophied. Another form of anacrotie pulse is found in the ease of aortic insufficiency, and in a traeing the auricular systole may appear as a wave preceding the ventricular upstroke. This is due to the faet that the aortic eontents never being really eut off from the ventricular, the aurieular systole is transmitted through the blood in the ventricle.

Venous pulse. — As we have seen, the pulse is normally extinguished in the capillary area owing to the state of tonic contraction of the smallest arteries or arterioles, but this restricted condition of the outlet under eertain circumstances may be in abeyance. If the chorda tympani nerve be stimulated the submaxillary gland secretes, and the small arterioles become dilated to allow of a freer supply of blood to the active cells, with the consequenee that the pulse reaching them from the arteries higher up is continued through the capillaries and so into the veins. Another form of "venous pulse," with a different underlying cause, is seen in the veins opening into the right auricle when the tricuspid valve is incompetent, the systole of the ventricle propagating a wave of blood through the right auriculo-ventrieular opening into the auricle and thenee into the veins. Again, variations occur in the inferior and superior venæ cavæ near the heart, due probably to changes in the auricular pressure, the influenee of respiration, &c.

Local dilatation of arterioles. — The arterioles regulate the supply of blood to the capillary districts, and their local dilatation or contraetion gives rise to eertain general and local effects. The general effect on the vascular system of a local dilatation will obviously be a fall of pressure elsewhere, whereas a local constriction will lead to a general rise. The local effects of dilatation are hyperæmia of the part to which the arterioles in question are distributed, a rise in the capillary pressure, and, under certain conditions, a pulse which is transmitted to the veins. The temperature of the part also rises, and if the tissue be young and growing it may grow more rapidly.

The **main characters of the pulse** to be attended to are— (1) The rate; (2) the strength; (3) the rhythm—whether regular

or irregular; (4) the compressibility; (5) the volume; and (6) the character of the tracing.

When the amount of blood in an organ is increased or diminished, as during the systole and diastole of the heart, corresponding changes occur in the general volume of the organ, and various instruments are in use for determining the amount of the change. The *plethysmograph* has been devised for recording the changes in the "volume pulse," and its principle has been applied to the study of changes in the volume of such organs as the kidney and spleen in another form of instrument, called an *oncometer*.

Fig. 195 shows the method of using the plethysmograph in recording the volume pulse of the arm, but the same method may be applied to smaller parts, such as the fingers and toes. The limb is enclosed in a chamber containing fluid, and the movements

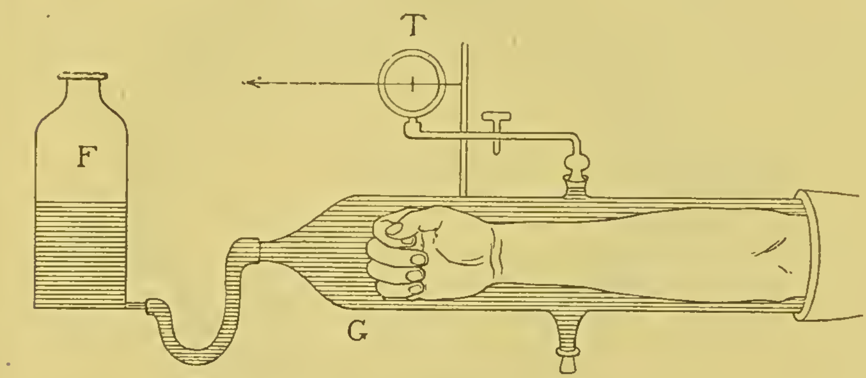

Fig. 195.—Mosso's Plethysmograph.

G, Vessel for holding limb; *F*, flask for varying water pressure in *G*; *T*, recording apparatus.

of the fluid—of increase during systole and decrease during diastole—are transmitted through a tube leading to an air tambour connected with a lever, or to a second chamber in which a piston and lever work. The resulting tracing on blackened paper presents much the same features as the ordinary pulse tracing, showing a primary wave with a dicrotic notch on the descending limb.

When this method is applied to the kidney, Roy's oncometer is used, and the resulting tracing is called an oncogram. The fluid, in this case oil, is separated from the kidney by a delicate membrane, but with this exception, and that of the use of a somewhat elaborate apparatus for recording the changes in volume by

a piston and lever arrangement connected with the oil of the oncometer by a tube, the instrument is an adaptation of the plethysmograph.

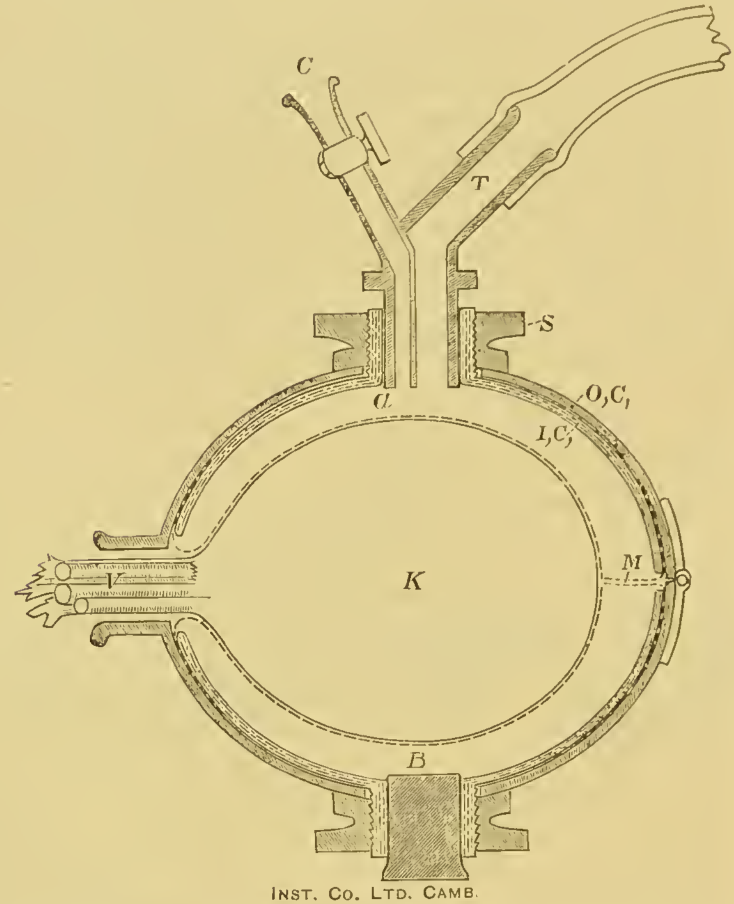

Fig. 196.—Roy's Oncometer (Renal)—Semi-diagrammatic Section.

K, Kidney; *V*, vessels and nerves imbedded in fat, &c., entering hilus of organ; *O.C.* and *I.C.*, outer and inner metal capsules screwed together by the screw *S*, and holding between them the edge of the membrane *M*, which applies itself to the surface of the kidney and forms with the metal capsules two chambers, *a* and *B*, the former of them communicating by a tube, *T*, with the recording instrument: *a* is filled with oil through *C*, and *B* through the opening *B*, closed with a plug in the figure.

With the plethysmograph not only can the pulse changes be recorded, but the tracing can also be made to show the effect of respiration, of contraction and relaxation of the muscles of the arm, and of the contraction of muscles in other parts of the body on the volume pulse.

The *compressibility* of the pulse varies from soft (pulsus mollis) to hard (pulsus durus). In a hard pulse the mean pressure is high and the vessel distended; in a soft, the mean pressure is low and the vessel relaxed. The *strength* of the pulse is indicated by the amount by which the blood pressure is increased at the point in question by the pulse wave. It may be estimated by means of the sphygmometer, an instrument which consists of a small indiarubber bag fixed to the lower end of a glass tube, which expands above and is closed at the top by a stop-cock. The bag is filled with coloured fluid, which on pressure passes up the tube, which is graduated in millimetres of mercury pressure. The whole is fixed to the wrist by a clamp, and the indiarubber bag pressed upon the radial artery. The air in the tube acts as an elastic cushion. The bag must be pressed upon the artery so as to elicit the greatest amount of oscillation of the fluid in the tube. The point of maximal pulsation gives us the arterial pressure, *i.e.*, the mean pressure, for it is when the pressure is the same on each side of the arterial wall that the latter vibrates most freely.

The other characters of the pulse have already been discussed.

The Blood-Stream.

We now come to the consideration of the *velocity of the blood*, which, as has already been pointed out, is to be distinguished from that of the pulse wave. The rate of the stream depends on three main factors—the original impulse derived from the heart, the resistance the blood encounters in the vessels, and the united sectional area of the vessels. The sectional area, as we have seen, may be represented by two cones placed base to base; the apices corresponding, the one to the commencement of the aorta and the other to the terminations of the venæ cavæ, the bases representing the capillary area. In the pulmonary circulation the one apex would correspond to the pulmonary artery, the other to the pulmonary veins, and the bases to the alveolar capillary net-work. But the apex of the cone representing the venous end of the circulation is wider than that of the arterial end, the sectional areas of the venæ cavæ being together greater than that of the aorta, and that of the veins generally greater than that of the arteries at the corresponding point. When fluid is driven through a channel (or a system of channels) its speed is inversely proportional to the width of the bed, and hence we find that the rate of flow in the arteries is greater than that in the capillaries, and that that in the veins occupies an intermediate position. The

following three velocities are given as occurring in a mammal of fair size, such as a large dog:—

In the carotid artery,	300 to 500 mm.	per second.
In the capillaries, - -	·75 mm.	"
In the jugular vein, - -	200 mm.	"

But it is to be noted that the flow is not uniform throughout either the arterial or venous systems. Thus it decreases in speed from the aorta, in which it is most rapid, as the terminations of the arterial tree are reached; and increases in the veins, from the smallest venules, as the heart is again approached. So that in speaking of the rate of flow in the arteries or veins, we are either speaking of the mean rate through a certain length of vessel or the exact speed at some particular point. In other words, the rate is not uniform throughout either tree, but varies inversely with the sectional area of the vessels; and it is a matter of common observation, indeed, that in a river the current is slower where it widens, and becomes more rapid where it narrows. The same amount of fluid having to pass each point in the river in the same time, it follows that it must flow more rapidly through the narrow part than through the broad, and more slowly through the broad than through the narrow.

That the slowing of the stream in the capillaries is due to the increased friction which the blood encounters in passing through so many smaller channels, and that the increased rapidity in the veins after the capillary area is passed, is due (*inter alia*) to the friction being removed, is at first sight a simple and attractive theory, but it does not seem tenable on more close examination; for the friction resistance in the capillaries would tell backwards upon the blood in the arterial system generally, and affect its rate at any point equally, so that for the differences in speed at different points of the arterial tree we are thrown upon the difference in the width of the bed above. Nor does there seem any reason for attributing the recovered speed in the venous radicles to the disappearance of the friction in the capillaries. In short, though the friction of the blood in the capillaries no doubt influences the rate of the stream through them, it is a factor which must influence the rate of the circulation as a whole rather than in one particular part alone.

In addition to the force of the heart—the *vis a tergo*—acting through the arterial tree and capillary plexus upon the blood in the veins, some other forces come into play to aid the flow of blood in the veins. *Muscular contraction*, by subjecting the veins to pressure, forces the blood in the only direction the valves will

allow it to take, *i.e.*, towards the heart. The *aspiration of the thorax* during inspiration also draws the blood in the venæ cavæ in the same direction. The heart also in expanding after its systole has theoretically the same influence, but practically this is too small to be of account.

Various instruments have been devised for estimating the rate of the blood current at a particular point. One of the earliest of these was Volkmann's *hæmadromometer*, which consisted of a long glass tube filled with normal saline and bent into the form of

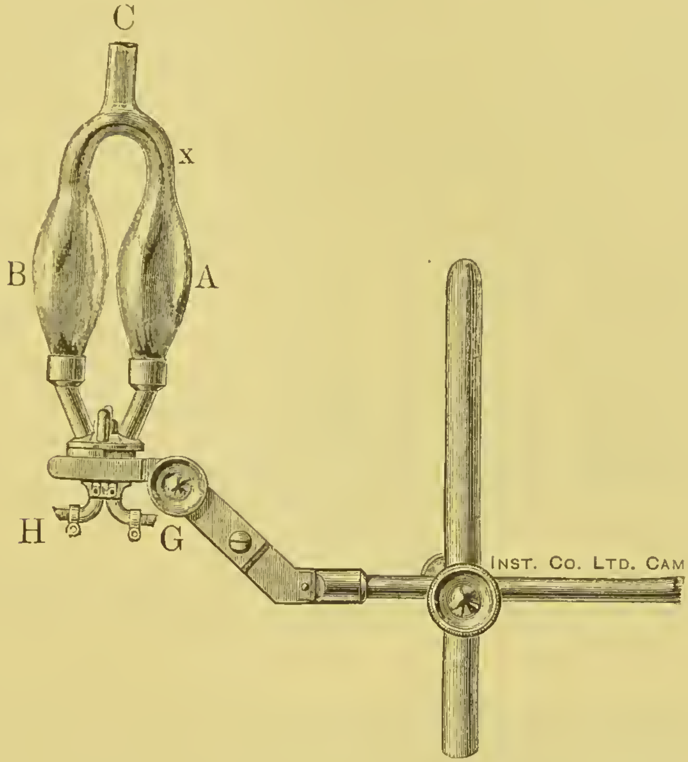

Fig. 197.—LUDWIG'S STROMUHR FOR MEASURING THE RATE OF BLOOD FLOW THROUGH AN ARTERY.

a U. This is placed upon the course of a vessel, blood is admitted at the proximal end by turning a stop-cock, and the time required for the blood to pass from one end of the tube to the other is noted. The length of tube divided by the time for the passage of the blood gives the velocity. In such an arrangement there are obvious sources of possible error, such as the width of the tube, its rigidity and length, &c. Ludwig's *stromuhr*

is in most common use. It consists of two glass bulbs, B and A, which open into each other, and the common tube C above, from which they are filled. By their lower ends they are fixed in a metal disc, through which they are in communication with the tubes H and G, which are to be connected with cannulæ fixed in the proximal and distal ends of a severed blood-vessel. The disc can be rotated through two right angles so as to reverse the connection between the bulbs and the cannulæ, in one position B being connected with H, and in the other with G. If turned through one right angle alone the bulbs are entirely shut off from the tubes, which then communicate with each other. In using the instrument the bulbs are thus first shut off, the bulb A is filled with olive oil up to the mark x, and the rest of the instrument (including bulb B, the remainder of A and the two tubes, H and G) with defibrinated blood. The tubes H and G are then connected with the cannulæ in the artery, H with the distal and G with the central end. The bulbs are then turned through a right angle, so that the tube G opens into bulb A. The clamp on the central end of the vessel is then relaxed and blood flows into the bulb A, displacing the oil, which is driven over into bulb B, the common tube C being of course closed. When the blood reaches the point x (the level previously reached by the oil), the bulbs are rotated through two right angles, so that bulb B (now filled with the oil that was in A) is put into communication with the tube G. The blood now sends the oil back into A, and the fresh blood in A follows the previous defibrinated blood into the distal end of the artery. As soon as blood has entirely replaced the oil in B, the bulbs are again turned through two right angles, and the process is again and again repeated for a certain time, usually till through clotting or otherwise the apparatus fails to work.

The amount of fluid necessary to fill A up to the mark x has been previously determined, and if the number of times the bulbs have been turned during the course of the experiment be noted, the calculation of the amount of blood flowing through the vessel is simple. If 5 cc. (bulb A up to x) have passed through G twenty times in 100 seconds, 1 cc. flowed through in one second.

Now the velocity of flow at a cross section may be regarded as the volume of fluid passing in a unit of time divided by the cross section of the current. If the diameter of the vessel be 3 mm., its sectional area will be 7·06 sq. mm., and 1 cc., or 1000 cmm., divided by 7·06 = 141·6 mm. per second as the rate of flow.

Another method of estimating the rate of flow is by means of *Chauveau and Lortet's* improvement of *Vierordt's hæmatachometer.*

A brass tube with a membrane covered aperture in its side, mid-way between the ends, is fixed in the usual way in the artery, the blood-flow in which is under examination. A lever pierces the membrane, which acts as the fulcrum—the short arm of the lever, expanded at its end, projecting into the blood-stream, and the long arm outside the vessel. The excursion of the lever is in proportion to the rate of flow of blood, and its movement may be estimated by means of a scale, as shown in the figure. It is more useful in the study of the relative rate of the blood-stream during

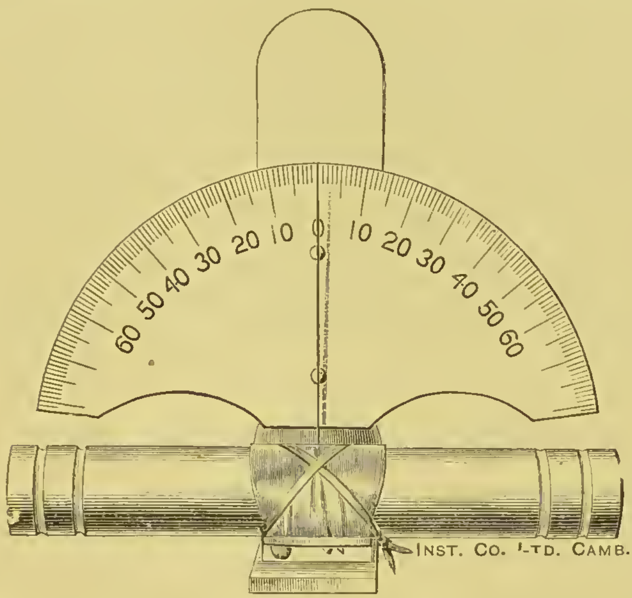

Fig. 198.—Hæmatachometer of Chauveau and Lortet for Measuring the Blood Current in an Artery.

the systole and diastole of the heart than for determining the absolute velocity, for which the stromuhr of Ludwig is of more practical value. Chauveau's instrument may be adapted so that the lever writes on a moving surface and records the *velocity pulse*, *i.e.*, a curve in which the changes in the rate of flow during the cardiac cycle are recorded instead of the movements of the vessel wall. The curve shows much the same features as the ordinary sphygmograph tracing—a sudden systolic rise with a dicrotic notch on the descending limb. The velocity pulse may also be recorded by means of the *gas tachograph*. The plethysmograph, already described, is connected with a gas burner. As the part enclosed in the instrument expands, the air issuing through the connecting tube causes the flame to rise; as the air is drawn

into the plethysmograph (when the volume of the part decreases during diastole) the flame sinks, its movements being photographed on a travelling surface.

The *circulation time.*—The time required by the blood to complete the vascular circuit may be estimated by injecting a solution of potassium or sodium ferrocyanide into the jugular vein of one side and noting the time it takes to reach the jugular on the other side. The salt will necessarily have passed through the right side of the heart to the lungs, from the lungs back to the left ventricle, thence by the carotid artery to the capillary area of its distribution, and thence through the other jugular to the point of issue—the whole course of the vascular system. Without considering the details of the experiment, we may say briefly that the moment when the salt reaches this point is determined by the blood giving the Prussian-blue reaction with ferric chloride. The method has the disadvantage that the experiment cannot be repeated on the same animal. Another method of a somewhat similar nature is to inject methylene-blue solution into the jugular vein on one side and note the time when the injection becomes visible through the wall of the carotid on the other, thus obtaining the circulation time through the lesser or pulmonary circuit, which is short compared with the whole circulation time; and the method may be applied to ascertain the time the blood takes to pass through any organ, such as the kidney, liver, &c. Another method, devised, like the last, by Professor Stewart, is known as the electric method, and is undoubtedly the most valuable one we have. In it a portion of the carotid is laid upon platinum electrodes and connected through them with a Wheatstone's bridge, of which it forms one of the resistances, and through it with a Daniell cell, an induction machine arranged for the interrupted current, and a telephone. The secondary coil is moved sufficiently away from the primary to give the minimum sound of the telephone. If a 3 per cent. solution of common salt be now injected in small quantity into the jugular vein, when it reaches the carotid artery the resistance in the portion of it between the electrodes is lessened, the balance of resistance in the Wheatstone bridge is altered, and the sound of the telephone is increased. The observation consists in noting the time space between the injection of the salt and the increase in the sound of the telephone. A galvanometer may be substituted for the telephone arrangement, when the time is marked by the deflection of the galvanometer needle, in which case the interruptor is unnecessary, and the platinum electrodes may be changed for non-polarisable clay ones. The telcphone is, however, the more satisfactory.

This method has the great advantage that it may be repeated again and again on the same animal and a mean observation made, and it is readily applied to the determination of the circulation time of particular organs. In a rabbit, by this method, the time occupied by the passage of the blood from the jugular vein to the right femoral artery may be put at 5·4 seconds; from the jugular vein to the right femoral vein at 8·4 seconds; through the lungs 2·8 seconds; through the liver 3·9 seconds; through the kidney 10 seconds, longer, that is to say, than through any other organ, for the blood has here to pass through more than one set of capillary vessels. The total circulation time in certain animals seems to be about five or six times that of the pulmonary circulation time, which in the case of the rabbit would make it about 14 or 16 seconds. But the pulmonary circulation time varies with the size of the animal, and in man may provisionally be reckoned at from 12 to 15 seconds. If we take the lowest of those figures and multiply it by 5, the total circulation time in man will be at least 60 seconds, *i.e.*, a blood-corpuscle occupies 60 seconds, or one minute, in passing through the entire circuit.

Blood-Pressure.

We have already shortly referred to the blood-pressure in considering the vascular system in some of its mechanical aspects,

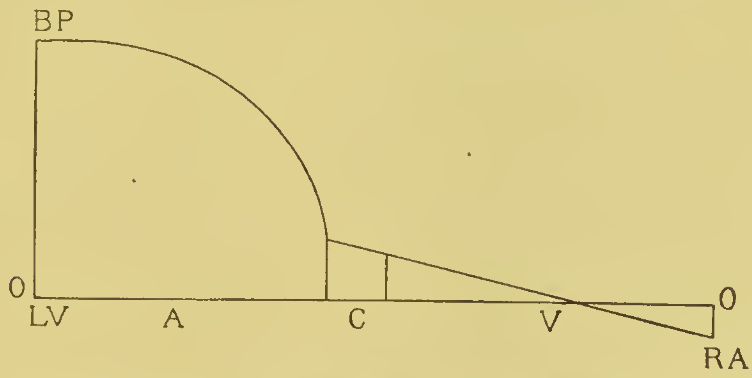

Fig. 199.—Scheme of Blood-Pressure.

Showing the amount in left ventricle, arteries, capillaries, veins, and right auricles. *O O*, Line of no pressure.

and we shall now consider it in a little more detail. By "blood-pressure" is meant the pressure exerted by the blood upon the wall of the artery, capillary or vein, as the case may be, and

this will obviously depend on the amount of blood the vessel contains relative to its capacity; and this itself is determined, other things being equal, by the relation between the inflow and outflow, depending on the force of the heart and the resistance in front. The latter is greatest in the arterioles and capillaries and we consequently find the pressure greatest in the arterial system. It diminishes from the heart onwards, being less in the smaller arteries than in the aorta, less in the capillaries than in the smaller arteries, and less in the veins than in the capillaries. Fig. 199 shows diagrammatically the fall in pressure along the systemic system, in which it will be noted that the great drop takes place just at the end of the arterial tree, at the commencement of the capillary area, from which point it falls gradually until in the veins in the chest the pressure is distinctly negative during inspiration, owing to the influence of the expanding thoracic wall on the thin-walled venæ cavæ.

The amount of the **arterial blood-pressure** was first measured by Hale's method, in which the blood is allowed to rise in a vertical glass tube in connection with such a vessel as the carotid, the column supported representing the pressure within the vessel. Poiseuille's advance on this method consisted in the use of a mercurial manometer—a U-shaped tube containing mercury—in place of the vertical glass tube; and this method, with improvements by Ludwig and others, is still adopted, but it is more useful for the study of the mean pressure and the more gradual changes in it than for recording the blood-pressure curve itself. For this purpose one of the spring manometers already mentioned (page 179) is more serviceable, as the mercury by its inertia is unable to follow and record the rapid changes in pressure which take place during the cardiac cycle. The mercurial manometer is used as follows. The U-shaped tube is filled with mercury up to the level of 10 or 12 cm. in each limb, and the remainder of its proximal limb with a saturated solution of sodium bicarbonate, *i.e.*, an innocuous solution which will retard the coagulation of blood, and a piece of strong rubber tube attached to this limb is filled with the same fluid, the tube being then clamped at the end. The carotid artery is exposed, clamped, and divided on the distal side, and a cannula, with a piece of indiarubber tubing on it, fixed in the clamped end of the vessel. The cannula and tube are now filled with the carbonate solution and connected with the manometer by a piece of glass tubing, which has also been filled with the solution, care being taken that there is no air in any section of the apparatus. The rubber tubes

should be strong pressure tubes to avoid any waste of force in expanding them, or the connection between the cannula and manometer may better still be made with a flexible leaden inexpansible tube. In each case, by means of a side piece connected with a pressure bottle containing sodium carbonate solution, which may be raised and lowered at pleasure, a pressure in the manometer a little greater than the anticipated blood-pressure is obtained before the clamp is removed from the artery. In this way the blood is kept within the arterial system and prevented from entering the cannula when the clamp is removed. The mercury in the open limb of the manometer bears on its surface a float and writing-style which is adjusted against smoked paper on a revolving drum. On opening the clamp in the artery the mercury in the manometer commences to oscillate and the style describes such a tracing as is shown in the accompanying figure. Here the larger curves are of respiratory origin, the mean pressure rising during inspiration and falling during expiration, while the small oscillations are due to changes in the arterial pressure during the systole and

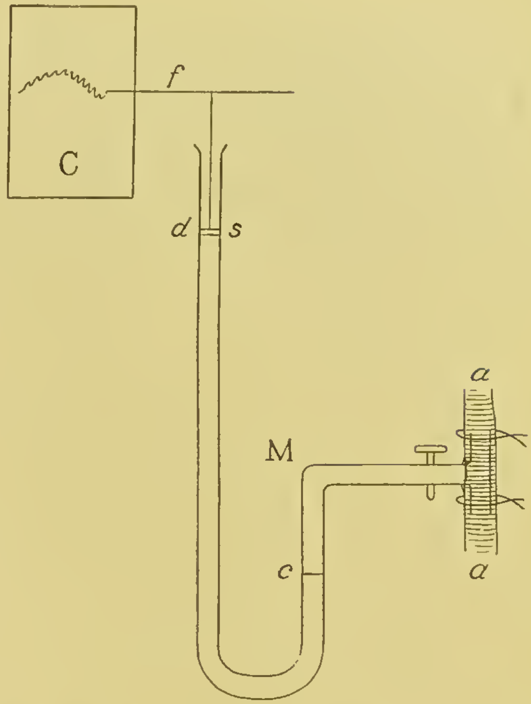

Fig. 200.—Diagram of Ludwig's Kymograph.

a, Artery; *f*, writing-style, supported by float *d s*; *C*, cylinder; *c*, level of mercury in shorter limb of manometer *M*.

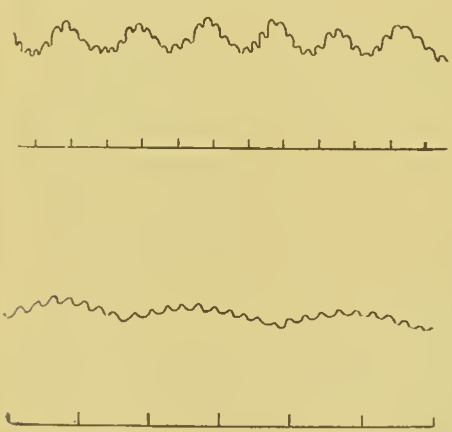

Fig. 201.—Blood-pressure Curves from the Carotid of Rabbit, the Time Marker in each Case Marking Seconds.

diastole of the heart. They are small, not because of their being really insignificant, for the rise in pressure during the systole may equal a considerable proportion of the minimum pressure, but because the inertia of the mercury prevents it recording rapid variations. The *maximum pressure* in such a tracing is indicated by a line joining all the maxima, the *minimum* or *permanent pressure* by a line joining the minima, and the *mean pressure* by a line "drawn between them in such a way that of the area included between it and the blood-pressure curve as much lies above as below it."

Stimulation of the depressor nerve of the heart.—The superior cardiac branch of the vagus, called the "depressor nerve," is, as we have seen, the sensory nerve of the heart, and on stimulation of its central end, pain and a well-marked fall of blood-pressure results, and it is from this latter, its chief function, that the nerve takes its name. It acts as a regulator between the heart and the peripheral resistance. When the latter is high the increased pressure in the heart stimulates the afferent fibres of the nerve, which transmit the impulses to the vaso-motor centre in the medulla, whereby the vessels, in the splanchnic area especially, dilate and the general blood-pressure falls, relieving the heart struggling against peripheral resistance in much the same way that amyl nitrite does. We shall return to this influence of the depressor nerve later, when the nervous control of the blood-vessels is under consideration. If the nerve be laid on the electrodes and stimulated with the interrupted current while the blood-pressure tracing is being taken with the mercurial manometer, a fall in the mean pressure results, as shown in Fig. 209. Otherwise the tracing is normal.

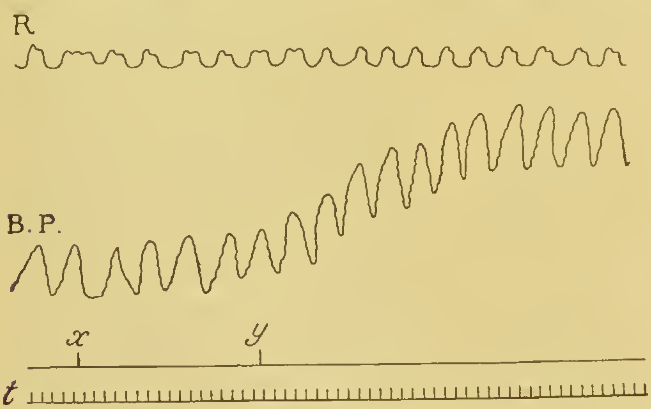

Fig. 202.—Effect on General Circulation—"press or effect"—produced by stimulating the central end of the Sciatic of Cat.

x, Stimulus sent in; y, shut off; R, respiratory curve; $B.P.$, blood-pressure; t, time in seconds.

Stimulation of an ordinary sensory nerve.—If the central end of the cut sciatic nerve be stimulated, the general blood-pressure

rises, owing to reflex contraction of the peripheral vessels—the typical result of stimulation of a sensory nerve.

Stimulation of the peripheral end of the vagus.—The result of stimulating the inhibitory nerve of the heart has features of particular interest. If the stimulus be a weak one, sufficient to produce slowing of the heart's action but not absolute stoppage, such a tracing as is shown in Fig. 203 is obtained. Here it will be noted that a very considerable fall in pressure takes

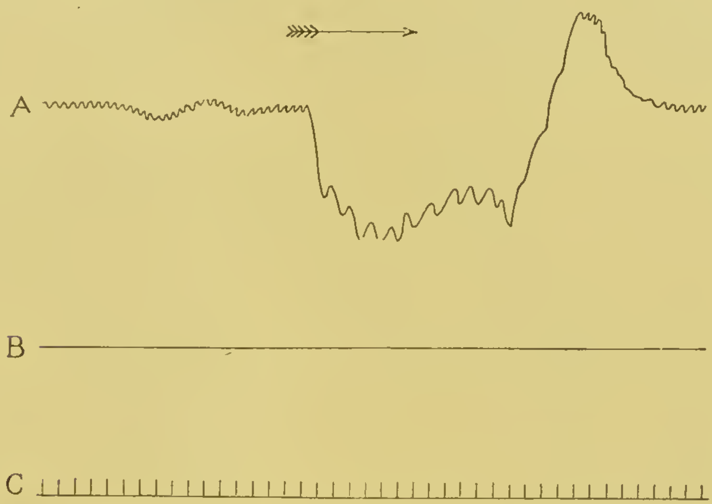

Fig. 203.—Effect on Blood-Pressure of Weak Stimulation of Peripheral End of Vagus (Rabbit).

A, Blood-pressure; *B*, abscissal line; *C*, time in seconds.

place while the stimulus is passing, and that during this time the excursion of the writing-style is largely increased. At first sight this would appear to indicate that the heart was beating with greater force than previously, but this is not the case, the apparent greater amplitude of the rise and fall being due to the slowing of the heart, which allows more time for the mercury to follow the variations of pressure, and thus shows how much more distinct the oscillations would normally be were it not for the inertia of the metal. When the stimulus is withdrawn the pressure is seen to rise considerably above the mean level for a time, and this is due to the increased rapidity and force of the heart's action following the restorative effect of the previous rest, but the pressure soon returns to its former normal level.

Fig. 204 shows the effect of a second stimulation of the nerve, and it will be observed that here the heart shows signs of impending escape from the inhibitory influence. The stimulus

employed in this experiment was stronger than in the previous one, and on its first application produced total inhibition except for one beat; but on its second it produced only slowing, and the pressure, which falls at the moment the stimulus is thrown in, rises again steadily from that point, till at the end of the stimulation it is well on the way again to the normal level. A third and a fourth stimulus would have shown decreasing effects, till finally no stimulation of the nerve would have influenced the heart's action or the blood-pressure. From this experiment we see, too, how much of the heart's work is spent in maintaining the mean pressure.

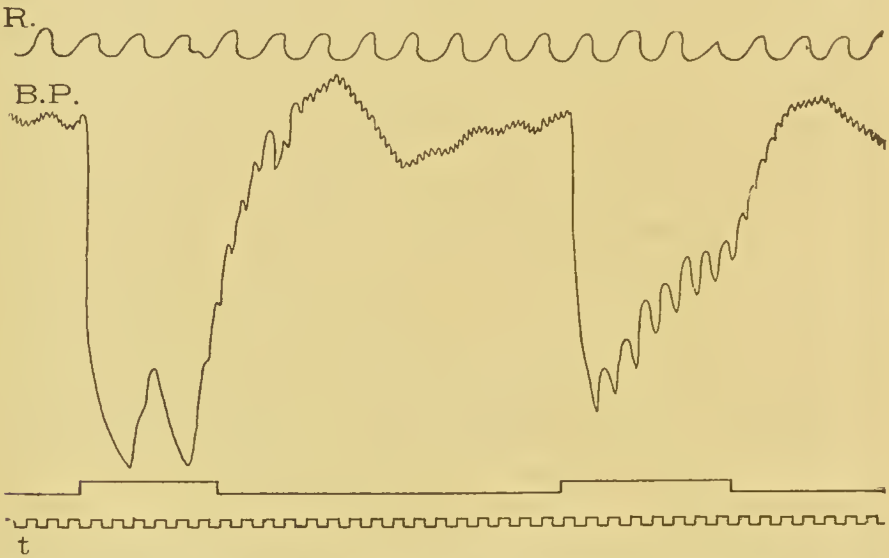

Fig. 204.—Two Successive Stimulations of the Peripheral End of the Right Vagus with the same Strength of Stimulus (Rabbit).

If the *central end of the vagus* be stimulated weakly, the first effect is the same as that of stimulating any nerve containing afferent fibres, such as the sciatic—the pressure rises; but if the strength of the stimulus be increased, reflex inhibition of the heart results and the pressure falls.

The above experiments will serve to show that the mercurial method of recording the blood-pressure is suitable for estimating the mean amount of it and the changes that take place in it as the result of stimulation of various nerves. The influence of other conditions may also be studied by it, such as asphyxia, action of drugs, &c.

But if we wish to obtain a tracing in which the individual phases of the pressure curve during the heart's cycle are shown,

the inertia of the mercury renders the method useless, and one of the spring manometers already mentioned must be used, such as the improved Fick, or Hürthle's spring manometer. Fick's original instrument consisted of a hollow C-shaped spring filled with fluid and connected by a tube with a cannula in the blood-vessel, a membrane closing the end of the spring and separating the blood and the fluid. Increase of pressure in the fluid in the spring causes it to open, and a decrease to close, and its far end records the movement through a system of levers connected with a writing-style. This instrument has been improved upon, and the pressure is made to work against a steel spring instead of the C-shaped tube (Fig. 206). In Hürthle's manometer the pressure is transmitted through a small drum to a steel spring which also acts as the writing-lever, the principle being the same as in the improved Fick.

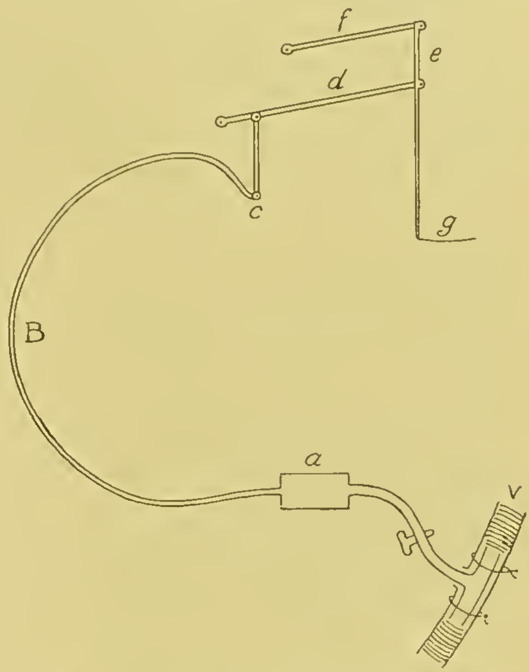

Fig. 205.—Fick's Spring Kymograph.

A hollow *C*-shaped metallic spring (*B*) is filled with alcohol. The distal end (*c*) of the spring is closed while the proximal end, covered by a membrane, is brought into connection with a blood-vessel (*v*) by a junction piece filled with a solution of sodium carbonate; as the pressure rises the spring tends to straighten itself, and so act on a series of levers, *d*, *f*, *e*, *g*. the point of the last of which writes upon a moving surface.

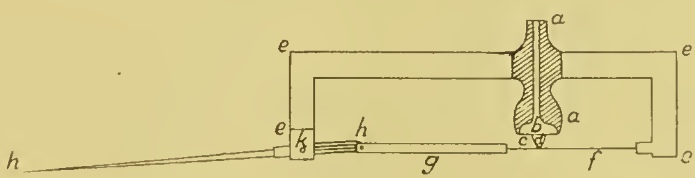

Fig. 206.—Fick's Spring Manometer.

aa, Tube opening into chamber *b* closed by the rubber membrane *c*; *d*, ivory knob in centre of membrane working on a steel spring *f*, the movements of which are exaggerated by the lever *h*.

A tracing taken with one of these instruments resembles very closely an ordinary sphygmographic tracing. Fig. 207 shows the events of the curve in detail, No. 1 being taken when the pressure was high and No. 4 when low, while Nos. 2 and 3 are intermediate. *p* Indicates the sudden systolic rise (which when the pressure is high (1) does not correspond with the highest point reached by the lever—see "anacrotic pulse"); *d*, the dicrotic wave; *a*, the dicrotic notch. Between *p* and *a* are seen secondary oscillations, one of which will be the predicrotic wave. Instruments for taking these tracings of blood-pressure are termed kymographs, and the tracings themselves kymograms.

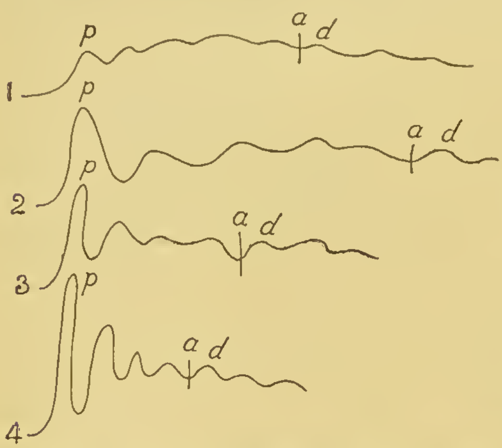

Fig. 207.—Blood-Pressure Tracings from Carotid of Dog, taken with Spring Manometer.

1, Taken when pressure was high; 2, pressure medium; 3, pressure low; 4, very low; *p*, primary elevation; *d*, dicrotic pulse wave; waves between *p* and *a* are systolic waves.

From a study of the last figure it will be seen that in whatever way the pulse is recorded — whether by means of the plethysmograph (volume pulse), the hæmotachometer of Chaveau (velocity pulse), the spring manometer (pressure pulse), or the sphygmograph itself—the essential features of the tracing obtained are the same, viz., a sudden rise, corresponding with the systole of the heart, and a slower fall, with secondary waves on the descending part of the curve, of which the dicrotic is the most constant; and these are also the features which are to be observed in the natural tracing obtained by allowing a jet of blood from a cut artery to spirt against a moving screen.

The mean arterial pressure in man lies usually between 100 and 200 mm., being about 140 mm. in the carotid and 110 mm. in the radial artery; these estimates, it is needless to say, being largely based on experiments on animals. In the rabbit, as we have seen, the mean pressure in the carotid amounts to some 70 mm. of mercury or 90 cm. of a column of blood.

Blood-pressure in the veins.—The pressure in the veins being so much lower than it is in the arteries, some lighter fluid, such as water, is used to record it. Unlike the arterial pressure

it decreases as the heart is approached, being about 3 mm. in the inferior vena cava as contrasted with 9 mm. in the smaller veins of the arm. In the thoracic portion of the veins entering the right side of the heart the pressure may be negative. Speaking generally, the pressure in the veins of a limb may be estimated at from $\frac{1}{10}$ to $\frac{1}{20}$ of the pressure in the corresponding arteries.

The **capillary blood-pressure** is estimated by the weight required to produce blanching of the part, and in this way the pressure in the capillaries at the root of the nail in man has been put at from 30 to 50 mm. of mercury. Such a method of course gives only an approximative result.

Various conditions affect the mean arterial pressure, some of the following being artificial or experimental, while others form part of the natural physiological scheme. In the first place, the force and rapidity of the heart's action is an important factor in the blood-pressure. The more vigorously the heart pumps blood into the arterial tree, the more blood this will contain at any given time (other conditions remaining the same) and the higher the pressure will be; and the more slowly and feebly the heart works, the less blood will be sent into the arterial system, and the lower the pressure will fall. Secondly, the amount of peripheral resistance will have an important influence. If the arterioles are constricted so that the outflow is diminished, more blood is heaped up behind the constriction than if they were relaxed and the outflow free; the blood-pressure consequently rising. Thus a strongly beating heart and a constricted state of the arterioles means a high pressure, and the reverse conditions a low one, but in health the condition of the heart and the peripheral vessels usually balance each other, so that a normal pressure is the result; a rapidly beating heart compensating a dilated state of the arterioles, for example, the adjusting mechanism being the cardiac and vasomotor centres in the medulla and their nerves to the heart and blood-vessels. Thirdly, the amount of blood within the circulatory system influences the pressure, and though this amount does not normally vary to any appreciable extent, its influence may be studied by artificially bleeding the animal or injecting fluid into its circulation; and such an experiment is instructive as showing the extent of the control of the nervous system over the heart and blood-vessels, whereby they can so adapt themselves to the amount of blood they contain that the normal mean pressure is maintained though the amount of blood is considerably varied. A dog may lose one-third of its blood without any marked change in the mean

pressure taking place, and similarly its blood may be increased in quantity to the extent of one-third without any lasting increase in pressure. This is due to the governing action of the cardiac and vasomotor centres in the medulla. When blood is withdrawn from the general circulation in any quantity the heart's action becomes more rapid and the peripheral vessels contract, so that the pressure is maintained though the amount of blood in the whole system is less; and similarly when blood is thrown into the circulation the vessels dilate readily to accommodate it, especially those of the splanchnic area, the watery part is quickly eliminated, and the mean pressure maintained. But this regulation by the nervous system does not follow either abstraction from or addition to the circulating fluid if the spinal cord be previously divided so that the cardiac and vasomotor centres in the medulla are cut off from the heart and blood-vessels. Of these three influences affecting the arterial blood-pressure, viz., the condition of the heart, of the arteries, and the amount of blood, it will be noted that the latter is normally constant, and that even when varied within considerable limits artificially, it produces little or no effect on the blood-pressure; whereas the action of the heart and the state of the peripheral arterioles are both very variable in health and from one moment to another under changing general conditions, and are the two main factors in the maintenance of the normal, or any change to a higher or lower pressure. Thus the arterioles may readily be dilated by taking a warm bath, or by inhaling nitrite of amyl, and in each case a temporary fall in the general arterial pressure takes place. Experimentally a similar result follows stimulation of the depressor nerve or section of the spinal cord in the neck (see "Vasomotor Nerves"). On the other hand, a cold bath, or the administration of digitalis, or stimulation of the vasomotor centre, will raise the pressure by constricting the peripheral arterioles.

Vasomotor Nerves.

We have seen that the heart is subject to both augmentor and inhibitory influences, reaching it by the sympathetic and vagus nerves respectively, the former increasing the contraction of the cardiac muscle and the latter diminishing or arresting it. In a somewhat similar way the arteries are under the control of the nervous system. No such influence is exerted upon the capillary vessels, nor, generally speaking, upon the veins, though the portal vein, which in many respects resembles an artery, is an exception to this rule. Of the arteries it is the smaller ones

—those in which, as we have seen, the muscular element is particularly predominant—that are most under nervous influence, and, by their contraction or relaxation, regulate the peripheral resistance. It may be again remarked here that such relaxation is as much a result of the activity of the muscle cell as its contraction, and is not merely the result of cessation of contraction. The *passive* state of the muscle cell is rather a condition midway between that of contraction and relaxation, the condition known as "tonic contraction," in which the small arteries in many parts of the body are usually found, and which takes its part in maintaining the general blood-pressure.

The constriction of the arteries or their relaxation plays a most important part in the physiological mechanism of the body. Thus, as we have already seen, the vessels require to accommodate themselves to the action of the heart and the amount of blood in them in order to maintain the mean blood-pressure; and in many other ways their dilatation or constriction, generally or locally, is an essential of the proper working of the animal frame. Thus when the body is exposed to cold the arteries of the skin contract, and so radiation of heat from the surface is diminished and the blood is withdrawn to more deeply seated parts to be kept warm. During digestion the mucous membrane of the stomach, in order that it may exhibit its full functional activity, requires to be freely supplied with blood, and this is attained through relaxation of its vessels' walls, the vessels of the skin becoming constricted to compensate for it, and hence the feeling of chilliness sometimes experienced after a full meal. In mastication of the food, the salivary secretion, which takes place freely at the time, necessitates a free supply of blood to the salivary glands, which is brought about by relaxation of their vessels. During muscular exercise the vessels supplying the muscles dilate, so that the circulation through them is temporarily increased. We might multiply such instances of constriction or dilatation almost indefinitely, but the instances already given will suffice for our purpose, and we have now to consider in some detail how these changes in the calibre of the vessels are brought about.

The nerve fibres passing to the muscular walls of the vessels are termed *vasomotor* fibres; those which transmit impulses leading to contraction being distinguished as *vasoconstrictor*, and those transmitting impulses causing dilatation as *vasodilator*.

The **vasoconstrictor fibres** arise from a bilateral centre in the medulla (the position of which has been defined by experiment), and, passing down the cord on the same side as that of the medulla from which they arise, leave it in the anterior roots

of the spinal nerves from the second dorsal to the second lumbar inclusive. From the anterior nerve roots they pass by the white rami communicantes into the sympathetic ganglia at the side of the spinal column, and thence to the vessels of the viscera by sympathetic branches or plexuses, or to other parts by joining the cerebro-spinal nerves. On leaving the cord the nerve fibres are medullated and remain so till they reach the ganglia, in which they lose their medullary sheath and arboresce round the ganglion cells, from each of which a new axial non-medullated process continues the further course of the nerve fibre to the vessel to which it is destined, in this way differing from the vasodilator fibres which, as we shall see, do not pass through the ganglia and retain their medullary sheath almost to their termination, at all events until they reach more distally placed ganglia in or near the vessels themselves. The path pursued by the vasoconstrictor fibres in any particular case is ascertained by experiment, of the nature of which the classical one by Claude Bernard on the *cervical sympathetic* may be taken as an example. In the ear of the rabbit there is a longitudinally running artery with its accompanying vein, which in an albino are very readily seen on holding the ear up to the light. The artery exhibits rhythmic contractions and dilatations sometimes, which take place at intervals of about a minute; or the rhythmical condition is absent, the artery being in a state of tonic contraction, *i.e.*, balanced evenly between contraction and dilatation. If the

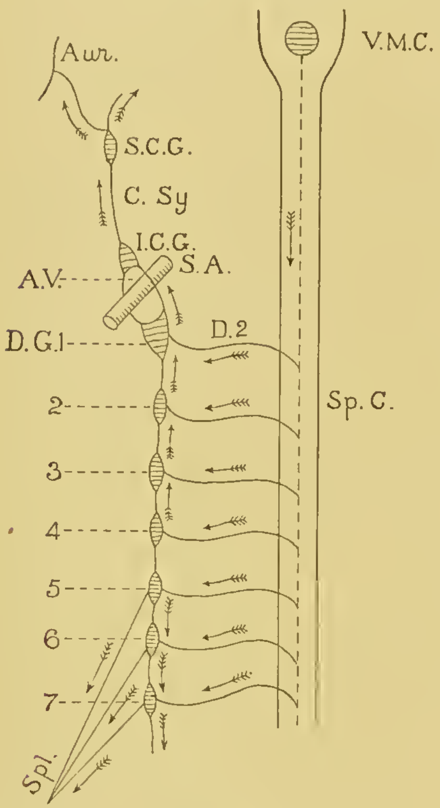

Fig. 208. — Diagram of Vasoconstrictor Fibres of Cervical and (part of) Dorsal Sympathetic.

V.M.C., Vasomotor centre in medulla; *Sp.C.*, spinal cord; *Aur.*, auricular artery; *S.C.G.*, superior cervical ganglion; *C.Sy.*, cervical sympathetic; *I.C.G.*, inferior cervical ganglion; *A.V.*, annulus of Vieussens; *S.A.*, subclavian artery; *D2*, second dorsal nerve; *D.G.1*, first thoracic ganglion; *D.G.2*, second thoracic ganglion; *Spl.*, abdominal splanchnic.

cervical sympathetic nerve be divided in the middle of the neck (see Fig. 208), the rhythmic movements if present cease, the vessels dilate, and the ear becomes warmer; it becomes hyperæmic, that is to say, and this without any alteration of the heart beat. From this it is clear that the vessels have been cut off from a tonic constricting influence reaching them constantly through the cervical sympathetic. In addition to the ear, some other parts of the head and face supplied through the same nerve are affected by its division, but this need not detain us here.

If now the distal, *i.e.*, the cephalic, end of the divided nerve be stimulated gently with the interrupted current, constriction of the artery of the ear results, so that both it and the vein visibly diminish in calibre and may become almost unrecognisable. The ear becomes colder, in fact a condition of anæmia has supervened, and the rhythmic movements of course are absent. The other parts to which the nerve is distributed show the reverse of the signs they exhibited before. Here we have clearly, then, an exaggeration of the normal action of the nerve. By making a series of experiments on different animals we can trace the fibres in the cervical sympathetic down past the first thoracic ganglion, through the second, third, fourth and fifth dorsal nerves into the spinal cord; division of these nerve roots having the same effect as division of the cervical sympathetic itself, and stimulation of them producing, as before, constriction of the vessels of the ear.

We have therefore in the cervical sympathetic an instance of a nerve in which the vasomotor fibres are of the sub-class vaso-constrictor only. As we shall see immediately, most nerves contain both kinds of fibres.

The effect of nicotine upon ganglion cells may be demonstrated upon the cervical sympathetic. As in the case of the heart (page 191) it is in the ganglia that the "block" takes place when nicotine is either injected into the circulation or applied locally, and it is probably the fine arborescing branches of the central nerve fibre around the ganglion cell which are paralysed. If the cervical sympathetic be divided in the neck and its peripheral (*i.e.*, cephalic) end stimulated, the blood-vessels of the ear become constricted. If now a one per cent. solution of nicotine be injected into a vein, and after an interval the nerve be again stimulated as before, no constriction of the vessels of the ear occurs; but if the nerve be stimulated on the other side of the ganglion (*i.e.*, between it and the distribution of the nerve), constriction results as before. This method is of great service in tracing the ganglionic connections of the fibres.

Even after the cervical sympathetic is divided in the first experiment, it is to be noted that in a considerable number of

cases the vessels of the ear ultimately recover their tone, at least to some extent, so that though the central nervous system undoubtedly exercises normally an important essential control of their walls, the muscle fibres would themselves appear to have an inherent tendency to return to the equilibrium of their normal tension, even when permanently cut off from central assistance; for in the case of the rabbit's ear there are no local ganglia which could be supposed to take on the function of the vasomotor centre.

Another instance of a purely vasoconstrictor nerve is to be found in the splanchnics, which supply the blood-vessels of the abdomen. If the *splanchnic nerves* be divided a sudden fall of pressure results from dilatation of the abdominal vessels, which have lost their tone. If the peripheral ends of the nerves be stimulated the vessels become constricted — more so than they are normally—and a corresponding rise in the general blood-pressure takes place; these changes in pressure ensuing because in the first case dilatation in the splanchnic area withdraws blood from the general circulation, while in the second, constriction in the same area increases the amount of blood elsewhere. Here, as in the rabbit's ear, the nerves obviously contain fibres which normally transmit impulses to the walls of the vessels they supply, maintaining them in a state of tonic contraction.

The course of the **vasodilator fibres** is a little different from that of the vasoconstrictor. They arise from a centre in the medulla (probably situated in the neighbourhood of the vasoconstrictor centre, though its limits have not been accurately determined by experiment), and passing down the cord leave it by the anterior roots of the spinal nerves. Their outflow does not seem to be limited to any special part, though their existence has been specially demonstrated in the nerves of the cranial and sacral regions. Unlike the constrictor fibres they do not join the sympathetic ganglia, but pursue a more direct course to their destination. Moreover, they retain their medullary sheath till they reach their termination or until they join some peripheral ganglion. They differ, again, from the vasoconstrictor fibres, which are constantly in action, maintaining a certain tone in the vessel wall, in having no such constant activity, being only thrown into action on special occasion through a mechanism to be presently considered. Moreover, their influence is more local and does not materially affect the general pressure.

We may now turn to the consideration of a purely vasodilator nerve—the *chorda tympani*. This is a small branch, springing from the facial or seventh cranial nerve, which joins the lingual branch of the fifth, and then leaving it is distributed to

the submaxillary salivary gland. The chorda tympani also contains secretory fibres for the same gland, which is supplied with vasoconstrictor fibres by the cervical sympathetic; but with the secretory and vasoconstrictor fibres we are not now concerned. If the chorda be divided no change results, but stimulation of the peripheral end has a very marked effect. The gland becomes hyperæmic, and if one of the veins issuing from it be cut, the escaping blood is arterial in colour and often shows a distinct pulse; the arterioles having been dilated to such an extent that the peripheral resistance at the arterio-capillary junction has disappeared and the pulse is carried through the capillaries and on into the veins. Of course, as is usual in these experiments, stimulation of the nerve produces an exaggeration of what normally occurs.

The dilatation here is not the *result* of the secretion which accompanies it, because if the secretory fibres be paralysed by atropin, dilatation still occurs on stimulation of the peripheral end of the cut nerve as before. We have then in this case to deal with fibres which when stimulated seem to exert a direct dilating effect on the vessel wall, and which are hence termed vasodilator.

Another instance of a purely vasodilator nerve is found in the *nervi erigentes* of the penis. If they are divided no effect is produced, but stimulation of the peripheral cut ends causes dilatation of the arteries of the penis and the consequent erection of that organ, the blood leaving it by the dorsal vein being almost arterial in colour.

But when we come to examine an ordinary cerebro-spinal nerve, such as the sciatic, we find that it contains both vasoconstrictor and dilator fibres. If the *sciatic nerve* of a mammal be divided, the small arteries of the skin of the leg dilate and the temperature between the toes rises; and, similarly, if the peripheral end of the cut nerve be stimulated, the vessels contract and the temperature falls. But if a few days be allowed to elapse after section of the nerve before the stimulus is applied, a different result is obtained, the vessels becoming dilated. This apparently contradictory result is due to the fact that when degeneration sets in the constrictor fibres lose their irritability first and hence the effect of stimulation of the dilators becomes apparent in the absence of the more powerful constrictors. In other ways too, the differing influences may be separated: cold depresses the constrictors more than the dilators, and hence the application of cold to the limb throws the constrictors out of action, so that when the nerve

has been only recently cut, stimulation of the peripheral end produces dilatation; again, if instead of using the ordinary interrupted current, the shocks are sent in at greater intervals—say of one second—the vasodilator fibres alone respond.

But the sciatic nerve supplies both the skin and the muscles, and whereas the vasoconstrictors preponderate in the branches to the skin, it appears that the vasodilators are more powerful in the muscular branches. If the nerve to the mylo-hyoid of the frog be cut, the vessels of the muscle dilate, and on stimulation of the peripheral end they dilate still more. That this is not dependent on the contraction of the muscle is shown by excluding the contraction in an analogous way to secretion of the submaxillary gland. On poisoning with curara the muscle will no longer contract when the peripheral end of the nerve is stimulated, but dilatation of the vessels takes place as before. The inference clearly is that the first dilatation on section of the nerve is due to the removal of the usual tonic influence of the constrictor fibres, and the further dilatation on stimulation to the more powerful action of the dilators. The reason for this greater dilator element in the muscular branches of the nerve may fairly be supposed to lie in the need for extra nutrition and removal of waste from the muscle during its contraction.

Having thus briefly considered the action of the vasomotor nerves on the blood-vessels, we may now pass to the consideration of how they are normally influenced through the vasomotor centre. As we have seen, the vasoconstrictor portion of it at least is automatic: that is to say, it exerts a constant influence without any impressions reaching it from outside; but this constant influence may be augmented or decreased reflexly, or it may be affected by the state of the blood or by emotion. We shall consider first the influence upon it and the vasodilator centre of impulses reaching them by afferent nerves. The *superior cardiac branch of the vagus* is the sensory nerve of the heart, and if it be stimulated an impression is conveyed to the medulla, inhibiting the vasoconstrictor cells presiding over the splanchnic area, with the result that the vessels of the abdominal viscera dilate and the general blood-pressure falls. The fall, however, is not sudden as in the case of stimulation of the vagus inhibiting the heart (*cf.* Fig. 203). But this inhibitory influence of afferent fibres upon the cells of the vasoconstrictor centre in the medulla is not confined to the depressor nerve. If any nerve of ordinary sensation, such as the *sciatic*, be divided and its central end stimulated, the result is a *local dilatation* of the vessels of the part supplied

by the nerve and a *general constriction* of the other vessels of the body, whereby the effect of the local dilatation on the general blood-pressure is more than counterbalanced and the local dilatation still further encouraged. This general constriction, evidenced by a rise of blood-pressure when the central end of such a nerve is stimulated, is due to stimulation of vasoconstrictor cells in other parts of the centre, and has been largely made use of in experiments to determine the position of the vasoconstrictor centre.

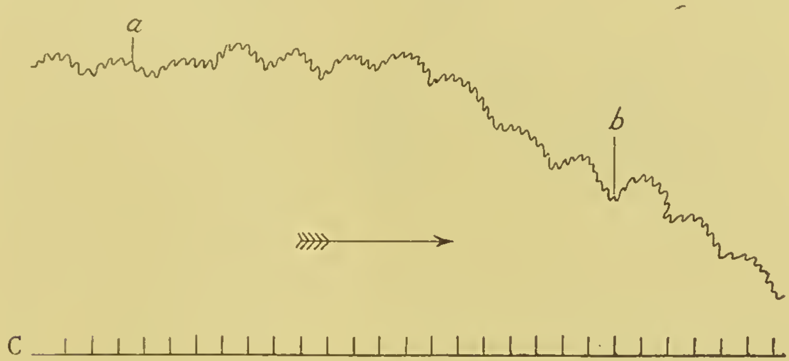

Fig. 209.—Stimulation of Central End of Depressor Nerve (Rabbit).

a, Point at which stimulation was thrown in; *b*, point at which it was shut off; note the time lost in development of effect, and the fact that the latter lasts after stimulation is over; *c*, time in seconds.

Another instance of the effect of stimulating the central end of a nerve of ordinary sensibility is afforded by the experiment of Bernard on the great auricular nerve of the rabbit's ear. If this nerve be divided no change in the calibre of the vessels of the ear takes place, and if the peripheral end be stimulated the result is the same, showing that it contains no constrictor fibres. But if the central end be stimulated the effect, as in the case of the sciatic, is both local and general. The vessels of the ear (after a transient constriction due to initial stimulation of the centre) dilate, owing to the inhibitory influence of the afferent fibres on the vasoconstrictor cells presiding over the area, and at the same time the general blood-pressure rises, due to stimulation of the cells in the constrictor centre which preside over the blood-vessels in parts other than those to which the great auricular nerve is distributed.

In the same way the gastric branches of the vagus, when stimulated by the presence of food in the stomach, convey inhibitory influences to the centre, whereby the gastric vessels are

dilated, while those of other parts, *e.g.*, the skin, become constricted through coineident stimulation of the cells in the constrictor eentre presiding over them.

But an afferent impulse may produce the same local dilatation in a different way: the afferent nerve for the salivary glands is the lingual branch of the fifth, and if it be stimulated by a drop of vinegar applied to the mueous membrane, the impulse passing to the medulla *stimulates* the vasodilator eells presiding over the fibres of the ehorda tympani nerve, and from them impulses are transmitted down the chorda, directly relaxing the museular fibres. Here, then, we have to deal with stimulation of vasodilator eells in the eentre, as contrasted with inhibition of vasoeonstrietor ones.

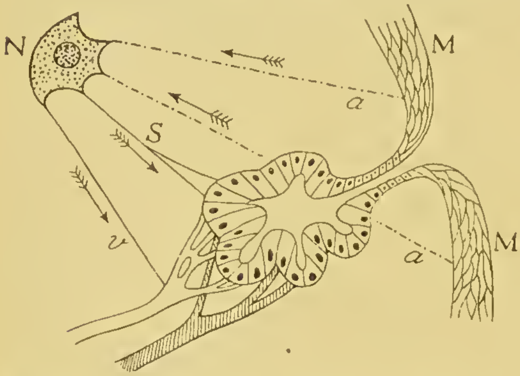

Fig. 210.—Diagram of Innervation of a Salivary Gland.

N, Nerve centre; *M*, mucous mcmbrane of mouth; *a*, afferent nerves from mucous membrane to nerve centre; *S*, secretory nerve from nerve centre to gland cells; *v*, vasodilator nerve from nerve centrc to blood-vessels.

Similar efferent vasodilator fibres are found in glosso-pharyngeal branches to the parotid gland, and in the ophthalmie division of the fifth to the eye and nose. Generally speaking, efferent vasodilator fibres are found in the anterior roots of the spinal nerves, whereas the fibres of the afferent nerves, in the reflex act, are found in the posterior roots. The anterior roots contain the efferent fibres produeing the seeretion of sweat, ordinary motor fibres to museles, efferent vasoeonstrietor and efferent vasodilator fibres; the posterior roots contain fibres of ordinary sensation, afferent fibres for the reflex eontraetion of muscles, afferent fibres for the reflex eonstrietion of blood-vessels generally and for reflex dilatation of the vessels in the area to whieh the nerve is distributed.

The **position of the vasomotor centre** has been determined by experiment. A manometer is plaeed in one of the larger arteries and some cerebro-spinal nerve, sueh as the sciatie, divided and its central end stimulated: a rise in the general pressure being the result. If the brain be now slieed away, from above downwards, it will be found that the reflex produetion through the eentre is not interfered with until the upper limit of the medulla is reaehed; that from that point downwards it becomes

progressively less on the slicing being continued, till a point is reached at which no stimulation of the central end of the sciatic has any effect. According to the result of this experiment, the lower limit of the centre is defined as being at a level of 4 to 5 mm. above the point of the calamus scriptorius, and the upper limit about 1 or 2 mm. below the corpora quadrigemina, and, as already stated, the centre is bilateral. Though we have spoken of this as the vasomotor centre, it is more the vasoconstrictor centre which has thus been defined, though, probably, the vasodilator centre has much the same position.

But though the general centre is located in the medulla, it seems probable that subsidiary centres exist in the cord. In the frog, if the slicing be continued still further downwards, a continuance of the lessening of the effect of stimulating the sciatic can be obtained; and in the mammal, after section of the cord in the dorsal region, the resulting dilatation of the vessels of the hind limb passes off after a time; and this may be referred to the existence of subsidiary centres in the cord, for stimulation of the central end of the sciatic will produce dilatation reflexly through the cord below the point of section. Again, in the case of the nervi erigentes of the penis, section of the cord above the lumbar region does not prevent erection taking place reflexly as the result of stimulation of its sensory surface, but this cannot take place if the lumbar part of the cord be destroyed; the inference being that a local centre for the vasodilator fibres exists in this part of the cord. At the same time, though subsidiary centres may and do exist in the cord, the centre in the medulla is the great ruling one.

We have seen that it may be affected in various ways reflexly through stimulation of afferent nerves, but it may also be affected by emotion or the state of the blood. The effect of emotion will be familiar to everyone: blushing and pallor of the face are both produced by the direct effect of mental processes on the cells in the vasomotor centre presiding over the fibres supplying the head and face; in the one case inhibiting the vasoconstrictor cells and in the other stimulating them; in each case the cervical sympathetic being the nerve involved. The vasoconstrictor centre is stimulated by the venous state of the blood in asphyxia, the blood-pressure rising till paralysis of the centre ensues; but though the vessels of the splanchnic area are constricted, those of the skin are dilated, especially of the face.

Vasomotor nerves of the veins.—The veins have plexuses of nerve fibres in their walls, like the arteries, but the extent

to which they are under nervous control is not yet definitely known. The portal vein seems to be influenced in much the same way as an artery, receiving its vasoconstrictor supply from the splanchnic nerves, stimulation of these under favourable conditions leading to a diminution in its calibre. Also, if the liver be enclosed in a plethysmograph and the central end of the cut sciatic stimulated the organ decreases in volume. As we said before, the portal vein in many ways resembles an artery and we cannot infer from its nervous relations similar relations in the case of other veins.

The Chemical and Physical Characters of the Blood.

We have already considered the morphology of the red and white corpuscles and we shall now turn to some of the general properties of the blood. Fresh blood varies in colour from bright red in the arteries to a purple-red in the veins. The colour is due to the pigment contained in the corpuscles which float in a fluid, the *plasma* or *liquor sanguinis*, which is almost colourless. Normally the blood is opaque, even in thin layers, but may be rendered transparent by various agencies, of which the addition of ether or water may be taken as examples. It is then said to be "laky," and the result is due to the pigment being dissolved out from the red corpuscles and diffused in the surrounding fluid.

The average specific gravity of the blood is from 1055 to 1060, and it may be estimated by allowing drops of blood to fall into fluids of known specific gravity. When the drop neither rises nor falls, the specific gravity of the blood is the same as that of the fluid used. This method has yielded interesting results in the hands of Lloyd Jones.

The reaction of blood is slightly alkaline owing to the presence of acid sodium phosphate and sodium carbonate. It varies in degree however, under different circumstances, *e.g.*, of digestion and muscular exercise.

The amount of blood in the body bears a fairly constant relation to the body weight, of which it forms about one-thirteenth.

Coagulation of blood.—The most notable property of blood is its power of coagulating after it is shed. In a period varying from three to ten minutes blood "clots," as it is called, that is to say, it first sets to a jelly which more gradually contracts and expresses a light straw-coloured fluid, the *serum*, which is almost free from corpuscles. Under the microscope the clot consists of a fine network of fibrils in which the corpuscles of the blood, red

and white, are entangled. Thus the blood, the clot, the serum, and the corpuscles have the following relations to each other :—

Blood...... { Plasma......... { Serum. / Fibrin } ; Corpuscles .... } Clot.

The fibrils consist of a substance chemically known as *fibrin*, and as no such fibrils are to be found in uncoagulated blood, the study of coagulation comes to be an inquiry as to the source of the fibrin and the means by which it becomes separated from the plasma, for we may say at once that it is not derived from the corpuscles; for if clotting be delayed in freshly drawn blood and the corpuscles separated from the plasma, it will be found that coagulation may be induced in the latter if the conditions preventing coagulation be removed. For instance, if the blood of a horse, which clots slowly, be run into a vessel surrounded with ice coagulation is greatly delayed, as cold retards it, the corpuscles sink to the bottom and the plasma can then be removed with a pipette; or the addition of a saturated solution of magnesium sulphate to the blood will similarly prevent coagulation, and the corpuscles may then be separated with the centrifugal machine. In the classical experiment of Hewson, the jugular vein of a horse is tied in two places and the piece excised; the blood remains fluid for a long time and the corpuscles have time to sink, but this method, needless to say, has not much practical application in the laboratory. But in any of these cases if the cause inhibiting the coagulation be removed (*e.g.*, if the temperature be raised sufficiently, or the salted plasma diluted with water) coagulation takes place and the clot contracts and expresses the serum as before; so that we are driven to the conclusion that in the formation of the clot the plasma supplies the material for the production of the fibrin. But though this substance is derived from the plasma we shall find that the white corpuscles of the blood play an important part in its separation. Hydrocele fluid consists mainly of blood-plasma, that

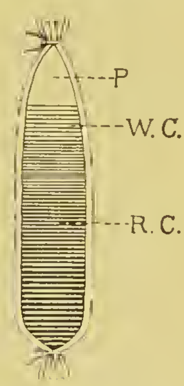

Fig. 211.—Hewson's Experiment with Vein of Horse.

P. Plasma; *W.C.*, white corpuscles; *R.C.*, red corpuscles.

is to say, it contains the substance or substances which are the precursors of fibrin, but it will not coagulate spontaneously. If now the serum of clotted blood be added to it it clots at once; or a piece of the clot itself from coagulated blood, even after it has been washed, will have the same effect. Clearly, therefore, some element exists in the serum of clotted blood, and in the clot itself, which is the *initiating* factor in the deposition of fibrin from the plasma.

The different parts of a clot are not necessarily alike in character, and this is well seen in the case of horse's blood, which clots slowly. If some horse's blood be placed in a cylindrical vessel and allowed to stand, the red corpuscles being the heaviest will sink first, and the white intermingled with some of the red form what is termed a "buffy coat" above them, the whole, when the clot contracts, being covered by serum. That is to say, that in this case the slowness of the coagulation affords time for the corpuscles to arrange themselves according to their respective gravity. If experiments on hydrocele fluid be made —(1) with the deeper redder part of the clot, (2) with the buffy coat, (3) with the serum, it is found that the part containing the white corpuscles, *i.e.*, the buffy coat, is the most effective in producing coagulation of the fluid.

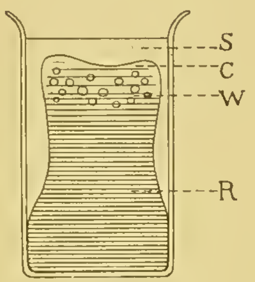

Fig. 212.—Beaker Containing Clot of Horse's Blood, showing "Buffy Coat."

S, Serum; *C*, cupped surface of clot; *W*, region of white corpuscle; *R*, region of red corpuscle.

The reason why all these parts produce coagulation is that a ferment—the "fibrin ferment" as it is called—is found in all of them, and by its action on the precursor of fibrin in the lymph or plasma leads to the production of the fibrinous network; and the buffy coat is the most effective part, as it contains the most white corpuscles, from which the fibrin ferment is derived. This ferment is not present in healthy living blood, but is the result of disintegrating forces acting on the white corpuscles and probably the blood-platelets. That it is a ferment is inferred from the fact that it does not become used up in the process of coagulation, and that a solution of it is rendered ineffective by boiling. Chemically it belongs to the class of nucleo-proteids and may be prepared from any tissue containing leucocytes in large quantity—such as the thymus or lymph glands—by extracting them after death with an 8 per cent. solution of sodium chloride. It may also be obtained by adding excess of alcohol to

defibrinated blood and allowing the whole to stand for a few weeks; the proteids are coagulated by the alcohol, and on extracting the precipitate with water the ferment passes into solution. It is this being in solution in blood after it is shed which renders any part of the clot or serum efficacious in inducing coagulation in the hydrocele fluid in the experiments mentioned above; and the buffy coat, composed of disintegrating white cells and representing the factory from which the ferment is being discharged, is naturally the most effective part. The blood as it occurs in the vessels during life contains but little fibrin ferment, so that when it is run from the blood-vessels direct into alcohol but little of it is obtained. The blood should be first defibrinated by whipping so as to release as much of the ferment from the white corpuscles as possible.

We may now return to the consideration of fibrin and its precursor in the blood. Fibrin itself belongs to the class of coagulated proteids, and gives the general proteid reactions (page 3). It is fibrillar, not solid, in structure; insoluble in water, and nearly so in weak saline solutions. If plasma which has been obtained free from corpuscles in any of the ways mentioned above be saturated with sodium chloride a precipitate is obtained, the *plasmine* of Denis. If this be dissolved in water the solution will clot, but what is left of the plasma from which it was precipitated has lost the power of clotting. We conclude, therefore, that the fibrin is derived from something in this precipitate. Two substances are found in it—*serum-globulin* and *fibrinogen*—and these may be separated from each other by the difference in their solubility in sodium chloride. If this salt be added to a solution of the precipitate till 13% be present the fibrinogen will be thrown down; on further addition of the salt till a strength of 20% is reached the serum-globulin will be precipitated. The precipitate of serum-globulin is granular, as contrasted with that of the fibrinogen which is sticky, and a solution coagulates at a temperature of 75°C., as contrasted with 56°C., at which fibrinogen coagulates. Of these two substances, whereas serum-globulin will not coagulate, the precipitate of fibrinogen in solution may readily be induced to do so; and that it exists as fibrinogen in the blood is indicated by the fact that if the latter be heated to 56°C., the coagulating point of the separated substance, it loses its power of clotting. Moreover, plasma from which the fibrinogen has been removed by precipitation with sodium chloride will not clot. Fibrinogen is readily soluble in a dilute saline solution, and its conversion to fibrin under the action of the fibrin ferment appears

to be not merely a change from a soluble to an insoluble form but a splitting up into two substances—*thrombosin*, which becomes converted to fibrin, and *fibrino-globulin*, which remains in solution and appears to take no further part in the matter.

But though we have spoken of the clot as being produced by the action of the fibrin ferment on the soluble fibrinogen of the blood, there is a third factor in the process which is essential to it, viz., calcium—the presence of a salt of this metal is a *sine qua non* of coagulation. Its precise mode of action, however, is not yet clear. If oxalate of potassium, even in weak solution, be added to blood, the latter loses its power of coagulation through the loss of its calcium, which is precipitated as the insoluble oxalate; and the injection of commercial peptone into the veins of a dog, whereby its blood temporarily loses it coagulative power, appears to depend on the affinity of peptones for calcium salts.

Certain conditions hasten and others retard coagulation—(1) a favourable temperature (a little over that of the body); (2) contact with foreign matter—*e.g.*, the sides of the vessel into which the blood is poured thus provoke coagulation, and the smaller the vessel the more rapid is the clotting, from the greater proportionate surface of the blood exposed; if the sides of the vessel be coated with neutral oil the coagulation will be delayed. If blood be stirred up, or "whipped," as it is called, with fibrous twigs, it will clot more rapidly than if it had been left alone, and the fibrin as it is separated will adhere to the twigs, and it is removed from the blood in this way for use in the laboratory; (3) movement of the blood hastens coagulation, partly by exposing it to the influence of a greater foreign surface; and (4) the addition of calcium salts.

Conversely, coagulation is retarded by a low temperature, as we have seen, when the vessel containing the blood is surrounded by ice, when the delay may reach an hour or longer. The addition of neutral salts, such as sodium or magnesium sulphate, delays it. Contact with the vessel wall seems to have an influence in postponing coagulation. We have seen that if the jugular vein be tied in two places and the part excised, the blood contained in it will continue fluid for a long time, even 24 hours or more. And even if such a piece of vein be converted into a test-tube by cutting off one end, the blood still remains fluid and may be poured from one such living test-tube into another and back again without clotting resulting; and the same with serous fluids, such as the pericardial. This fluid, unlike that obtained from a hydrocele, will clot spontaneously if removed from the body immediately after death and exposed in a vessel; but if the pericardial fluid

be removed in the pericardial sac itself it will remain long uncoagulated if kept in its natural cup, but clotting ensues at once if it be transferred to another vessel. On the other hand, if the wall of the vessel be injured, as it is in atheroma of the arteries, a clot is liable to form, due to the injured part acting as a foreign body.

Blood-plasma and serum.—Of the whole weight of the blood the corpuscles, with the water they contain, form from one-third to a little less than one-half. The specific gravity of the plasma, freed from the corpuscles, is from 1026 to 1029. As we have seen, the *serum* is the plasma of the blood, minus the fibrin, which forms with the corpuscles entangled in it the clot.

In 100 parts of serum we find of proteids, .	8 to 9%
Fats, extractives, and salts, . . .	1 to 2%
And of water, ...	90%
	100

The proteids of serum are *serum-albumin*, *serum-globulin*, and *fibrin ferment*.

The gases of the plasma and serum are *oxygen*, *carbon dioxide*, and *nitrogen*, most of the oxygen being contained in the red corpuscles and the CO_2 in the plasma (see "Respiration"). The fats, which are present in small quantity only, are represented by *olein*, *stearin*, and *palmitin*, and the complex substance *lecithin;* the extractives by such substances as *urea*, *uric acid*, *creatin*, *sugar*, *xanthin*, *hypoxanthin*, &c.; the salts by sodium chloride with potassium chloride in much smaller quantity, in this way contrasting with the red corpuscles, in which the potassium salt is in excess of the sodium. The other salts of the serum are phosphates and sulphates.

For the chemistry of the red and white blood-corpuscles and their morphological characters, see pages 28–30; for the spectra of hæmoglobin and its derivatives, page 12.

CHAPTER VII.

RESPIRATION.

RESPIRATION consists in the gaseous interchanges between the organism and the medium in which it lives, CO_2 being given off and oxygen absorbed. The process in the unicellular amœba, and even in multicellular organisms of a simple type, is one of mere diffusion, but as soon as any degree of complexity of general structure is reached, special organs of respiration—the lungs in the case of mammals and birds, and the gills in fishes—become developed. The principle of all such mechanisms is virtually the same—a considerable capillary area is exposed to the oxygen-containing medium which is caused to circulate over it. Thus, in the case of fishes, the gills are highly vascular membranes, over which the oxygen-containing water is made to flow by swallowing movements, the constant and rhythmical character of which is responsible for the fish's reputation as a hard drinker; while the oxygen-containing air in the lungs of mammals (which are also vascular membranes) is renewed by alternate movements of inspiration and expiration—by the alternate distension and partial collapse of an organ, which in its lower development is merely an epithelium lined sac with very vascular walls. The blood circulating through the capillary area thus exposed to a current of the medium in which the animal lives discharges the carbonic acid received from the tissues through the thin epithelial membrane which alone separates it from the air or water, from which it in turn takes up oxygen. Returning from the lungs (or gills) to the heart it is distributed again to the tissues, where it parts with its oxygen and again becomes loaded with carbonic acid, the exchange again taking place through a thin capillary wall. Respiration thus is both *external* and *internal*, the former taking place in the lungs, and consisting in the acquisition of oxygen and the release of CO_2, which diffuses out into the air or water; while the latter consists in the handing on of the oxygen received to the tissues, and the taking up of carbonic acid in exchange.

Thus, instead of a simple diffusion taking place through the protoplasm of the unicellular amœba or the ectoderm of cœlenterates, the exchange of gases between the various parts of the

organism and the medium in which it lives is effected by the exposition of one part of its capillary area to a current of the oxygen-bearing medium. The existence of special organs, such as the lungs and gills, for this purpose, therefore, presupposes the existence of a vascular system to subtend their function, but a vascular system does not necessarily imply the existence of a special respiratory apparatus or the exclusion of other methods of respiration. In some *vermes* respiration takes place only through the skin, which is richly supplied with blood, and in the frog the skin has an important respiratory function as well as the lungs. In man, however, the respiratory function of the skin is so small that it may be entirely neglected.

The Respiratory Apparatus.

The respiratory tract commences at the nostrils and terminates in the alveoli of the lung. The pharynx continues the passage from the nose to the larynx, which forms the upper somewhat box-like end of the trachea. The trachea is about fonr-and-a-half inches in length and bifurcates at its lower extremity into two large bronchi, one for each lung, and each of these bronchi divides repeatedly into smaller and smaller branches which terminate in the air vesicles of the lung of its side. The air vesicles are in fact the terminal expansions of the tubes (*cf.* structure of secreting glands).

The **larynx** contains the organ of voice, and in this connection its chief anatomical features will be considered later; here it will be enough to say that it is partially closed above by the two vocal cords, the slit between these being called the "rima glottidis."

The **trachea** is lined by a mucous membrane internally and possesses a submucosa, in the outer part of which is placed a succession of cartilaginous rings. These are deficient posteriorly and consequently somewhat horse-shoe shaped. The *mucosa* is represented internally by a layer of ciliated epithelial cells, here stratified, with goblet cells which secrete mucin interspersed here and there: this rests upon a well-marked homogeneous basement membrane. Beneath or external to the membrane is a somewhat narrow layer of lymphoid tissue, bounded by another narrow layer of elastic fibres which run longitudinally and are thus seen in transverse section when the trachea is cut across. Outside the mucosa is the *submucous coat*, a somewhat loose layer of connective tissue supporting the acini of the mucous glands, and containing blood-vessels, lymphatics, and nerves. The gland vesicles are lined by short columnar or cubical epithelial cells,

and their ducts, lined by smaller cells, may be traced through the intervening adenoid and elastic layers till they open on the inner surface of the trachea, with the lining epithelium of which they become continuous. In the outer part of the submucosa is found the ring of cartilage, incomplete posteriorly where the deficiency is made up by transversely placed non-striped muscular fibres, which are placed between the ends, but internally to them. The fibres are attached to the ends of the horse-shoe and their function is doubtless to narrow the lumen of the trachea by bringing them

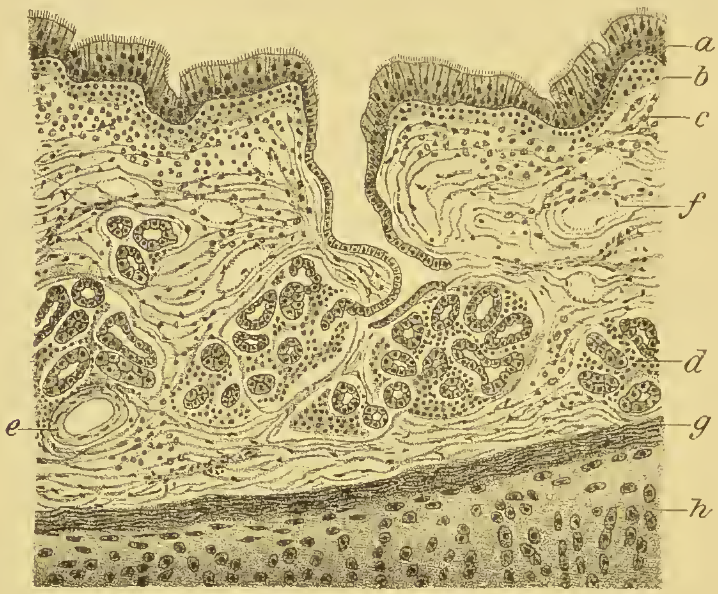

Fig. 213.—Transverse Section of Human Trachea.

a, Ciliated epithelium; *b*, adenoid tissue; *c*, elastic tissue; *d*, glands; *e*, blood-vessel; *f*, lymphatic; *g*, perichondrium; *h*, cartilage.

nearer together; or more generally speaking they provide the contractile element in this part of the respiratory tube, a feature which, as we shall see, is present in all the ramifications of the bronchi. The muscular fibres are not only found between the ends of the horse-shoe rings, but in the interspace between adjacent rings, so that they form a continuous transversely placed band through the length of the posterior surface of the trachea.

The cartilaginous rings are of the hyaline variety of cartilage, and are invested with a fibrinous perichondrium, which is continued as a sheet of fibrous tissue between the adjacent rings, the perichondrium of one thus running into that of another, and it fills

up the deficiency in them posteriorly, so that the fibrous tissue sheath of the trachea is complete. The bronchi, we have said, divide again and again, and a gradual transition takes place between the structure of the trachea and that of the smallest bronchial branches or bronchioles. It will be enough to describe the structure of one of the larger intra-pulmonary bronchi and that of the bronchioles in order to show the character of the change.

An intra-pulmonary bronchus, *i.e.*, a division of the tracheal tube within the lung substance itself, resembles the trachea in its general structure, but there are some points of minor difference. The horse-shoe-shaped cartilage is here broken up into three or more pieces placed in the outer part of the submucous coat or

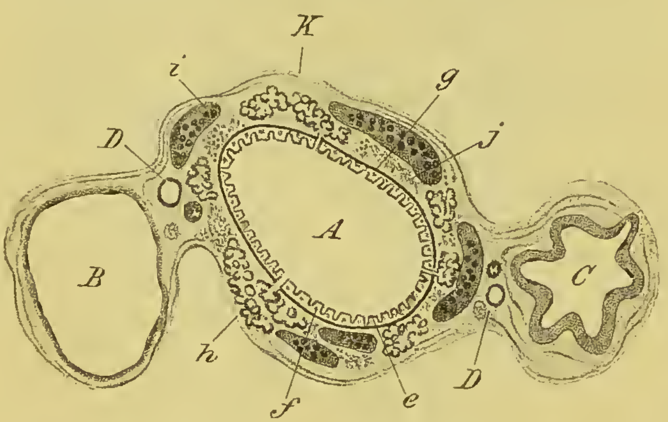

Fig. 214.—Semi-diagrammatic Representation of Intra-pulmonary Bronchus, with Pulmonary Artery and Vein, and Peri-bronchial Connective Tissue.

A, bronchus; *B*, pulmonary vein; *C*, pulmonary artery; *D*, bronchial vessels and nerve; *e*, epithelial lining of bronchus; *f*, adeno-elastic layer; *g*, muscularis mucosæ; *h*, mucous glands; *i*, cartilage plates; *j*, lymph follicular tissue; *K*, peri-bronchial connective tissue.

peribronchial tissue, which is continuous with the interlobular septa and through them with the pleura or fibrous investment of the organ. The strands of non-striped muscle which were found at the posterior aspect of the trachea are represented in the intra-pulmonary bronchus by a continuous narrow muscular coat, the *muscularis mucosæ*, marking the outer limit of the mucous membrane, and pierced by the gland ducts on their way to open on the lumen of the tube. Internal to the muscular is an adeno-elastic layer, the representative of the two distinct layers in the trachea, and lining this a layer of stratified ciliated epithelium which is found in longitudinal folds after death. The intra-pulmonary bronchus and its investing connective tissue corresponds to a

portal tract in the liver, and like the hepatic duct the bronchus is accompanied by blood-vessels. On one side of it is a branch of

Fig. 215.—Transverse Section of Intra-pulmonary Bronchus (Human) (× 300).

a, Ciliated epithelium; *b*, adeno-elastic layer; *c*, muscularis mucosæ; *d*, mouth of mucous gland; *e*, adenoid tissue; *f*, cartilage; *g*, mucous gland; *h*, submucosa.

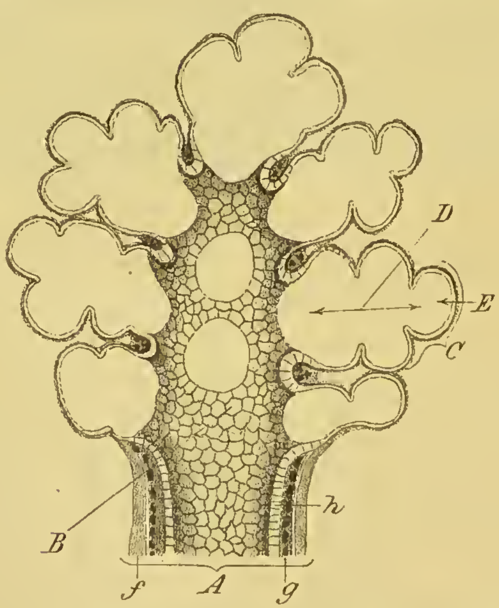

Fig. 216.—Diagrammatical representation of Termination of a Bronchiole in the Lung.

A, bronchiole; *B*, infundibular passage; *C*, infundibulum; *D*, alveolar passage; *E*, alveolus; *f*, connective tissue; *g*, muscle fibres; *h*, epithelium.

the pulmonary artery and on the other of the pulmonary vein, while in the outer part of the submucosa, external to the cartilage plates, are branches of the bronchial artery, vein, and nerve supplying the tissue of the lung itself.

As we follow the bronchial tubes onwards to their smallest divisions, the bronchioles, the cartilage plates and the mucous glands disappear, while the muscularis mucosæ still remains well marked and even persists in the infundibular passage in which the tube terminates. The wall of a **bronchiole** consists from within outwards of three layers—(1) a single layer of cubical epithelial cells, (2) a circular layer of non-striped muscle, and (3) connective tissue sheath. It terminates in an *infundibular passage*, *B* (Fig. 216), which is merely a continuation of the

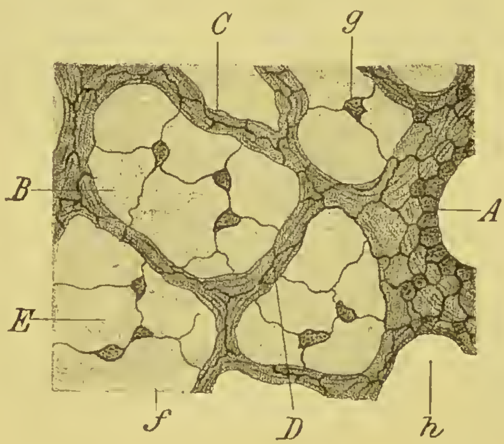

Fig. 217.—Section of Lung of Kitten.

A, Bronchiole; *B*, *E*, alveoli; *C*, *D*, alveolar walls; *g*, small granular cells; *h*, alveolus cut in plane above level of floor.

bronchial tube in a perforated state. The apertures lead into *infundibula*, *C*, the wall of which is made up of a number of cup-like expansions outwards, the *alveoli*, *E*. But whereas the wall of the infundibular passage is still composed of the three layers which are found in the smallest bronchioles, the alveoli present a marked change in structure. The cubical epithelial cells of the bronchiole are here expanded into large flattened plates, with here and there smaller granular germinal cells between them, the muscularis mucosa has entirely disappeared, and the fibrous investment is represented by a thin layer of elastic tissue supporting a capillary network which is joined by the terminal branches of the pulmonary artery and vein. The wall of the alveolus is thus very thin and only the

epithelium of the capillary and the large flattened cells of the the alveolus itself intervene between the blood-stream and air.

Fig. 218.—Section of Injected Lung of Human Fœtus.

Vascularisation of the lung.—The pulmonary artery enters and the pulmonary vein leaves the lung at its root and both accompany the bronchi in the peribronchial tissue. When the vesicular terminations of the bronchial tube are reached the artery breaks up into the capillary network which ramifies in the alveolar wall, in traversing which the blood loses its carbonic acid and takes up oxygen, the vein receiving the oxygenated blood and carrying it back to the heart. The bronchial artery arises from the aorta, and, unlike the pulmonary, brings arterial blood to the lung for the supply of its tissue. It enters the lung at its root, and accompanying the bronchi in their ramifications its branches break up into capillaries for the supply of the blood-vessel walls, the connective tissue of the bronchi, the interlobular septa, and pleura, the blood for the most part being returned by the branches of the bronchial vein, which, like those of the artery, lie in the peribronchial tissue. But the blood of the bronchial artery from the capillaries in the mucous membrane and the air passages has connections with the pulmonary system and is returned to the heart by the pulmonary vein: this is the explanation of the congestion and catarrh of the bronchial passages which is common when the return of blood by the pulmonary vein is hindered in lesions of the heart.

The **connective tissue of the lung.**—The lung is invested by a fibrous capsule, which is called the *pleura*, from which a sheath of tissue enters the organ with the blood-vessels and bronchi at the root to form the supporting framework of the lung. This sheath provides the peribronchial tissue already referred to, from which septa pass into the pulmonary substance to join those from other bronchial tracts or from the inner surface

of the pleura itself. In short, the connective tissue of the lung follows in its arrangement that of glandular organs generally (*cf.* "Liver").

The **lymphatics of the lung** are those of the pleura, the interlobular septa, the peribronchial tissue, and the alveolar wall. The whole organ is invested with the pleural sac, comparable to the pericardial investment of the heart, the two layers,

Fig. 219.—Section of Human Fœtal Lung, showing the Relations of the Different Parts of the Fibrous Framework to each other.

a, Visceral layer of the pleura; *b*, peribronchial connective tissue; *c*, interlobu connective tissue; *d*, small intrapulmonary bronchi; *e*, pulmonary artery; *f*, pulmonary vein; *g*, bronchiole within a lobule, expanding into *h* alveoli.

visceral and parietal, meeting over the vessels and tubes at the root. The sac is lined by large polygonal nucleated squamous cells, amongst which are numerous orifices or *stomata* guarded by smaller cells. The lymphatics of the alveolar wall are necessarily merely lacunæ in the elastic network, whereas anastomosing lymphatic spaces lined by sinuous epithelium are found in the pleura and peribronchial tissue and septa in addition to the cell spaces of the tissue itself. From the pleural sac the lymph passes by the stomata into the lymphatic spaces and channels of the pleura, thence to the interlobular septa, the peribronchial

tissue, and the alveolar wall. From all these sources it is carried by thin-walled lymphatic vessels to the bronchial glands at the root of the lung, and thence to the thoracic lymph trunks, and so into the general circulation.

The free communication between the lymphatics of the various parts of the lung may be readily illustrated by the conduct of foreign particles which enter the alveoli. Thus, in the case of anthracosis, or coal-miner's phthisis, the inhaled carbon particles pass between the epithelial plates of the alveoli and entering the lymphatic spaces of the alveolar wall pass thence to every part of the lung, so that upon section it may present a uniformly black appearance. In less marked cases the course of the pigment may be traced in the lymphatics of the deeper looser layer of the pleura, in the interlobular septa and peribronchial tissue, and in the lymphatic glands at the root of the lung.

The effect of respiration on the flow of lymph in the lung is much the same as in the case of blood. As the chest expands in inspiration, the lymph in the thoracic vessels tends to be drawn towards the heart, and this acting backwards on the lymph in the lung favours its flow in the direction of the glands.

The **elasticity of the lungs.**—The pleural and pericardial sacs, with the anterior and posterior mediastina, constitute the thoracic cavity, and here the pressure is lower than that of the atmosphere, owing to the elasticity of the lungs; in virtue of which they tend, both during inspiration and expiration, to contract upon the air in the alveoli and thus to withdraw the pleural surface from the chest wall. This elastic tension of the lungs is one of the main factors in expiration when the inspiratory effort is over, and its value has been estimated by placing a cannula connected with a manometer in the trachea and puncturing the wall of the thorax. When the thoracic wall is thus opened, the pressure of the atmosphere is exerted on the pleural surface as well as within the alveoli; in other words, the pressure within and without the lung is equalised and there is nothing to prevent the elastic recoil of the lung tissue from having full play. In the dead body the pressure exerted by the retracting elastic lung measured in this way 7·5 mm. of mercury when the chest wall was previously unexpanded in the expiratory position, and 9 mm. when previously expanded in the inspiratory; and this pressure is the equivalent of the intrathoracic negative pressure which it exactly balanced.

If the lung substance itself be punctured instead of the chest wall, the pleural surface communicating with the puncture, the

lung collapses in the same way and from the same cause, the air rushing into the pleural cavity, so that there is nothing to interfere with the elastic retraction of the lung. Here, again, the equalisation of pressure within and without the lung allows the elasticity of the organ to have full play. Nor can any subsequent dilatation of the thoracic cavity dilate the lung, for as the air outside the body is in communication with the pleural sac through the respiratory passages, there is no tendency to the creation of a vacuum, and the surface of the lung is no longer drawn outwards with the chest wall.

But even in such cases the lung substance is never completely collapsed, and a portion of it will float in water, nor will any amount of compression deprive it of this quality, for after the compressing force is removed the elasticity of the alveolar walls comes into play in the opposite direction and a certain measure of recoil in the way of expansion takes place, whereby air again enters the vesicles. Before birth, however, the bronchi and air vesicles are undilated and the lung tissue is therefore solid, or "atelectic" as it is called, and pieces of it will sink in water; but after inspiration has once taken place this condition is never resumed. Until the first inspiration, *i.e.*, during embryonic life there is thus no negative pressure in the thoracic cavity, for the elastic elements in the lungs have not been yet put upon the stretch and consequently the lung does not tend to retract from the chest wall and to make a vacuum in the pleural cavity.

Development of the lung.—The lung is developed as a diverticulum from the anterior part of the alimentary canal and at first closely resembles a secreting gland. The alveoli are represented by glandular-looking vesicles lined by cubical epithelial cells, and the bronchi by ducts indistinguishable from those of an ordinary gland. It is only later that the ducts present the more complex structure of bronchial tubes, and not until birth, when the first inspiration is taken, that the cubical cells of the alveoli become expanded to flattened squames. But the general arrangement of the parts of the organ remains distinctly glandular.

The Mechanism of Respiration.

The end of the respiratory mechanism is the constant change of the air in the lungs, so that that which has become altered by the addition of carbonic acid and the loss of oxygen may be expelled and fresh air introduced in its place. Ventilation of any

chamber may be effected by either of two methods—(1) The withdrawal of air already in the chamber, its place being taken by incoming fresh air, and (2) the forcing in of fresh air; in the one case the pressure being lessened at the outlet and in the other increased at the inlet. In mammalian respiration the first of these methods is adopted, fresh air being *drawn* into the lungs via the nose, pharynx and larynx by diminishing the pressure in the alveoli, so that fresh air flows in till the pressure in them equals that of the atmosphere; but in the frog air is *forced* into the lungs by closure of the mouth and nostrils, followed by the contraction of the muscles of the floor of the mouth, whereby its cavity is reduced and the contained air forced on into the lungs.

In mammals the pressure of the air in the alveoli is reduced, and so an indraught through the respiratory passages secured by expansion of the thoracic cavity. The way in which this acts on the lungs is very easily demonstrated by means of an apparatus such as is shown in Fig. 220. B is an air-tight glass vessel, closed below by an elastic membrane, M, to the centre of which a string, S, is attached. Above, it is closed by an india-rubber stopper, perforated to allow of the passage of a tube communicating with an elastic bag, L. B represents the thoracic wall, L the lung, M the diaphragm, and the space between B and L the thoracic cavity, or, for simplicity, we may say the pleural space. As we shall see immediately, the diaphragm is not the only factor in the enlargement or diminution of the thoracic cavity, the chest wall itself taking its part; but for the purpose of the demonstration it is indifferent how the change in the capacity is brought about. If traction be now made on the string, S, so as to stretch the elastic membrane, M, downwards, the pressure in the jar is reduced outside L, which dilates, air being drawn in through the

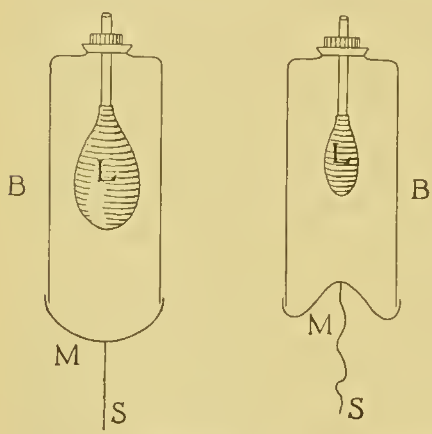

Fig. 220.—Scheme of Movements of Lung in Chest.

L, A thin elastic bag representing the lung and communicating with the outer air by a tube passing through the cork of the bottle *B*. *B*, Bottle without a bottom, the aperture being covered by an elastic membrane *M* tied on. When the membrane is pulled down by the string *S* (descent of diaphragm) the pressure of the external air causes *L* to expand; when the string is let go *L* contracts from its elasticity, and is still further diminished in size if *M* be invaginated from below.

tube to fill it. When the string is released the membrane resumes its former position, the pressure between the sides of the jar, B, and the bag, L, is increased again, the elasticity of the bag causes it to contract, and air is again forced out through the tube. In this experiment the pulling down of the string and the consequent increase of the capacity of the chamber B represents the muscular dilatation of the chest in inspiration; while the release of the string and the return of the membrane to its former position represents the actions of gravity and elasticity in expiration.

Further, if the membrane, M, be now forcibly invaginated from below, the bag, L, undergoes further diminution in size until the pressure on either side of its wall is equal, and on again releasing M from the force which displaced it the bag, L, will expand again till it reaches its original dimension. This corresponds to what happens in the living subject when, by a forced expiratory effort, the size of the chest has been diminished more than usual, its elasticity enabling it to recover its normal capacity, and the lung following it.

In the above experiment a distinct space filled with air exists between the elastic bag and the wall of the chamber containing it, but in the case of the chest no such space exists between the visceral and parietal pleural layers. These glide directly upon each other, only a little lymph to lubricate them intervening. This gliding movement is essential to secure the free working of such organs as the lungs and heart. If the surfaces of these organs were adherent to the inner surface of the chest wall they would be greatly hampered; that part of the lung, for instance, would dilate most which lay in the most dilatable part of the thorax, and *vice versa.*

We have now to examine how this dilatation and subsequent diminution of the thoracic wall in respiration is brought about. First we will consider ordinary respiration, for it is to be noted that when special respiratory efforts require to be made, as in running or in any other form of violent exercise, special muscles are brought into play which are at rest in quiet breathing.

Ordinary respiration.—In *inspiration* the chest cavity is increased in size in its vertical, antero-posterior, and lateral diameters. The vertical diameter is increased by the contraction of the *diaphragm*, a muscle which separates the abdominal from the thoracic cavity and projects like a dome against the lower surface of the lungs. When it contracts it is forced downwards, the angle which its sides make with the thoracic wall opens out, and it is closely followed in its descent by the lungs, which glide on

its surface as they do on the sides of the thoracic wall. This muscle is attached to the lower ribs, and during contraction its points of attachment are fixed by the action of the *quadratus lumborum* and the *serratus posticus inferior*.

Increase in the transverse and antero-posterior diameters of the chest is brought about by the *levatores costarum*, the *scalene muscles* and the *intercostals.* The scalenus anticus and medius by their contraction fix the first rib, and the scalenus posticus the second, and so afford a fixed point for the intercostal muscles to act upon. The levators costarum arise from the transverse processes of the last cervical and first eleven dorsal vertebræ, and are inserted between the tubercle and angle of the rib on the same side, immediately below their point of origin, and they are undoubtedly the most important factor in the raising of the ribs and the consequent increase in the diameter of the chest. The exact way in which the intercostal muscles act has been hotly disputed, the external intercostals and the intercartilaginous part of the internal being generally credited with raising the ribs when the two upper ones have been fixed by the scalene muscles, and according to some the interosseous part of the internal intercostals acts in the same way.

Another view is that the interosseous internal intercostals act only in expiration and help in depressing the ribs. The accompanying figure illustrates the supposed mode of action of the intercostals on this last hypothesis. On the right is shown the general principle that when the ribs are lowered from the horizontal, the line joining them vertical to their long axes is shortened, that is to say, the intercostal space is decreased, while as they rise towards the horizontal it is increased: and if they were to be further raised above the horizontal it would again lessen. But in the case of the intercostal muscles we are dealing with lines which run slantingwise in different directions, *gh* and *ik* representing the fibres of the interosseous external intercostal, and *lm*, *no*, those of the same part of the internal intercostal. A muscle shortens during its activity, and on

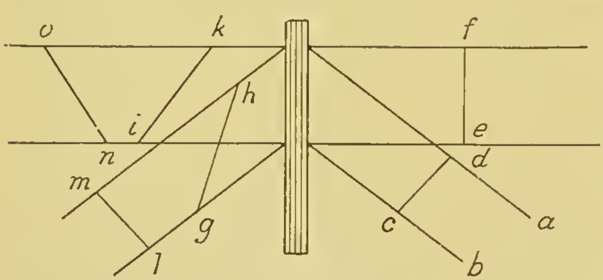

Fig. 221.—Diagram illustrating Action of Intercostal Muscles.

comparing the relative length of the slanting lines when the ribs are raised and depressed, *gh*, the external muscle, is seen to become shorter (*ik*) when the ribs are raised towards the horizontal; while *no*, the internal intercostal fibre, becomes shorter (*lm*) when the ribs are lowered. Fig. 222 shows the way in which the interchondral part of the internal intercostal acts differently to the interosseous—for though the direction of the fibres is the same in both cases, they are placed at the other side of the angle formed by the junction of the cartilage and the rib, and their mechanical relation to the cartilages between which they lie and the sternum is the same as that of the intercostal portions of the external muscle to the ribs and spine. In either case, when the ribs are raised, the diagonal of the rhomb, as shown in the figure, becomes shorter; and the diagonal represents the muscular fibre.

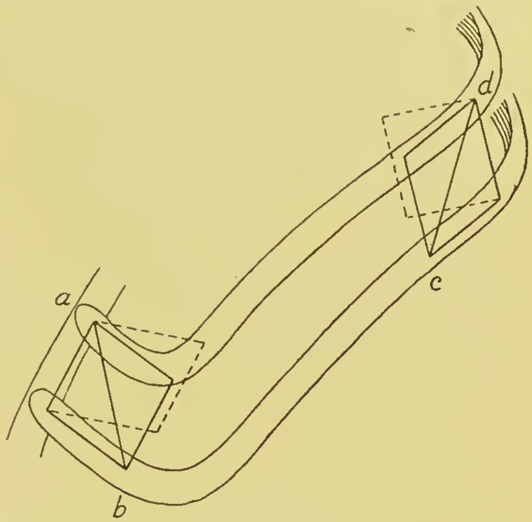

Fig. 222.—Diagram of Action of Intercartilaginous Portion of Internal Intercostal Muscles.

Scheme showing that when the ribs are raised the intercartilaginei (*ab*) and external intercostals (*cd*) are shortened. The diagonal of the rhomb in either position represents the muscular fibres.

It is only possible here to thus indicate briefly some of the considerations on which the discussion as to the precise mode of action of these muscles has been based, the question being a very complicated one, involving many mechanical details; but whatever view we take—whether we consider the one set of fibres to act in inspiration and the other in expiration, or that they both act during both phases, or in inspiration alone—when they do contract they will doubtless render the soft tissue between the ribs more tense during inspiration, and so prevent it being drawn inwards. If this, however, is their function in ordinary respiration, much more will their action be essential in both forced expiration and inspiration; in the one case to prevent the soft intercostal sheet being bulged outwards when the pressure within the chest is high, and in the other to prevent it being drawn inwards when it is

low. If the pulp of the finger be pressed upon an intercostal space and a forcible expiratory effort be made, the mouth and nose being closed, a very sensible hardening is felt of the tissue pressed upon, which is probably due to intercostal contraction.

The enlargement in the transverse and antero-posterior diameters of the chest, which takes place when the ribs are raised, depends on the fact that each succeeding rib (except in the case of the lower ones) is an arc of a larger circle than that immediately above it, and hence when those above are fixed in position and those beneath are lifted towards them the diameter of the chest is increased at any given point. The widening of the angle where the osseous and cartilaginous portions of the ribs meet, which accompanies the upward pull on them, also tends to increase the lateral diameter.

As the ribs are raised at the sides and in front by the muscles mentioned—posteriorly they are all fixed by their articulation with the spinal column—it follows that the sternum is raised and brought forward with them, especially at its lower extremity; its upper end, articulating as it does with the clavicles and the first and second ribs, being almost stationary.

In *expiration* in quiet breathing the chest returns to its previous dimensions without muscular effort of any kind. At the moment when the muscles concerned in the inspiratory effort relax, all the forces which have been overcome by the contraction of the diaphragm and the other muscles come into play. The chest wall sinks back, partly through its own weight, and partly from the elasticity of the twisted costal cartilages; the abdominal contents, displaced downwards by the contracting diaphragm, again press on the thoracic contents; the elasticity of the distended lung induces its shrinkage as soon as the thoracic pressure begins to rise.

Forced respiration.—In forced respiration many other muscles are brought into action, and these increase in number with the degree of muscular effort required. The muscles which may thus act are here given in a tabulated form, but it need scarcely be said that no good purpose is served by commiting such a list to memory.

Auxiliary Muscles of Forced Respiration.

A.—Inspiratory.

The upper ribs are elevated by.....	Scaleni. Cervicalis ascendens. Serratus posticus superior.

The hyoid bone is elevated by......	Genio-hyoid. Mylo-hyoid. Stylo-hyoid. Digastric.
The sternum is elevated by	Sterno-hyoid. Sterno-thyroid. Thyro-hyoid. Sterno-mastoid.
The shoulder bones are elevated and pulled back by	Trapezius. Levator anguli scapulæ. Rhomboideus major. Rhomboideus minor.
The ribs are drawn up to the elevated shoulder bones by ...	Serratus magnus. Pectoralis major. Pectoralis minor. Subclavius.
The lower ribs are pulled down and fixed (to enable diaphragm to act more powerfully) by	Serratus posticus inferior. Quadratus lumborum.

B.—Expiratory.

The abdominal viscera are pushed up against diaphragm by......	Obliquus externus. Obliquus internus. Transversalis abdominis. Levator ani.
The ribs are depressed by	Triangularis sterni. Rectus abdominis. Ilio-costalis. Longissimus dorsi.

(Rutherford.)

In *forced expiration* the *abdominal muscles* are much the most important factors, and act by compressing the abdominal viscera and forcing them against the retreating diaphragm, the *rectus abdominis* by its contraction depressing the ribs at the same time. In *forced inspiration* the *pectorals* are brought into play, the arms being fixed to give them a point to work from, and this is illustrated by the conventional method of holding the arms rigid and flexed, and the hands clenched in running. The *sterno-mastoid* helps to raise and fix the clavicle, and thus the upper part of the chest generally, the *trapezius* also raising and pulling backwards the shoulder bones, while the *serratus magnus* aids the pectorals in raising the ribs.

The muscles of forced expiration are more powerful than those of forced inspiration.

Types of respiration.—Respiration may be *diaphragmatic* (*i.e.*, abdominal) or *costal*, that is, the movement may be initiated by the descent of the diaphragm, which takes the most prominent part in producing the change in the capacity of the chest; or it may be started by the raising of the ribs and chest wall, the diaphragm completing the movement, and having a smaller share in the result. In animals, amongst the herbivora, the diaphragmatic type of respiration prevails; amongst the carnivora, the costal. In children the breathing is chiefly diaphragmatic or abdominal. In men it is chiefly diaphragmatic, but the inferior part of the chest is more involved than in children. In women the respiration is chiefly costal, and in them the upper part of the chest is especially involved in the movement. In forced respiration, the costal type prevails in men, women, and children, according to the extent to which the auxiliary muscles of respiration are brought into play.

It is a somewhat undecided question why the type of respiration should differ in men and women as no difference exists in children. Advocates of a more natural dress for women are not backward to seize upon the occasion and fasten the superior costal type of breathing upon the offending corset, which it must be admitted by all is calculated to exaggerate it. But the rise and fall of a woman's breast was a noticeable characteristic of the sex before tight lacing or corsets came into fashion, and we must perhaps look deeper for the explanation of the difference. In pregnancy, the abdominal cavity becomes largely filled up by the growing embryo, and the descent of the diaphragm proportionately difficult, and it is conceivable that the development of the costal type of breathing after puberty is a preparation to adapt the body to the physical changes in pregnancy. That in young children of either sex there is no difference in the type of respiration does not show that the difference in adults is not fundamentally a sexual one, for before puberty children are virtually asexual beings.

Movements of the glottis and alæ nasi.—In forced respiration, the glottis and alæ nasi widen in inspiration, and resume their previous position in expiration. The larynx also rises and falls synchronously with the chest.

Respiratory rhythm.—The frequency of respiration is about 15 or 20 per minute, but it varies with age, sex, and different conditions. In the new born child it may be 50 to 70 per minute, in one of two or three years of age 20 to 30 per minute. It is greater in females than in males, and is increased when the temperature is raised, and decreased in sleep.

The relative duration of the phases of expiration and inspiration is as 7 or 8 is to 6, that is to say that expiration takes a little longer than inspiration, and between the end of expiration and the beginning of inspiration there is a short pause, which, however, disappears if the breathing is at all hurried. No pause occurs between inspiration and expiration.

The respiratory rhythm may be recorded graphically by means of Marey's *stethograph*, the use of which will be obvious from the figure. It is fixed in position round the chest by the tape *e*, connected with the arms *d* and *c*. When the thorax expands in inspiration, the metal plate bends under the force exercised by the arms, and this affects the tambour *g* through the upright *b* to which it is attached; the air in the tambour communicating the movement through a tube *a* to a second tambour connected with a writing lever.

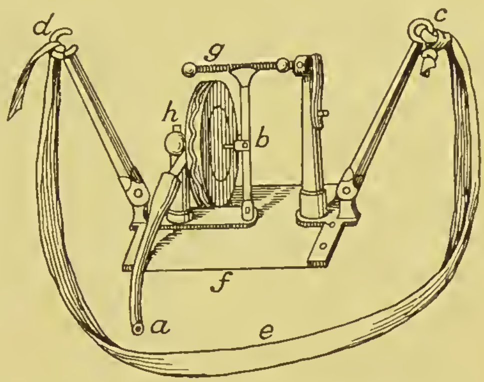

Fig. 223.—Marey's Stethograph.

There are other instruments devised on somewhat similar lines, such as Sanderson's and Brondgeest's, in each of them the essence of the apparatus being the same as that of Marey's stethograph, and the cardiograph previously described.

In animals, the rhythm may be recorded by placing an india-rubber bag, connected with a tambour and writing-lever by a tube, between the diaphragm and the liver; or the changes in the air pressure in the lungs may be made use of by placing a cannula in the trachea, and connecting it by means of a tube and breathing chamber with a tambour and writing-lever; or the pressure changes in the thoracic cavity may be recorded by the introduction of a cannula connected with a mercurial manometer into the pleural or pericardial cavity, air from outside being, of course, excluded; finally, a strip of the diaphragm may readily be semi-detached in the rabbit, and the record of its contractions and relaxations obtained by attaching it by one end to a writing-lever.

Fig. 224 shows a tracing obtained by means of a stethograph applied to the chest wall.

Respiratory sounds.—If a stethoscope be applied to the chest wall, certain respiratory sounds are to be heard which differ in

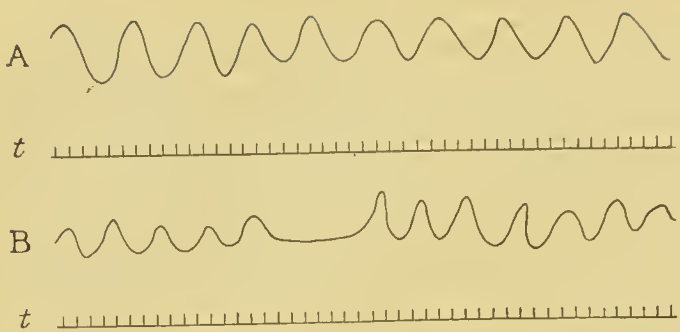

Fig. 224.—Tracing of Changes in Transverse Diameter of Thorax.

A, During quiet breathing; *B*, shows the effect of swallowing; *t*, time-tracing in seconds.

character according to the part of the chest wall selected for examination. If the spot selected be over a large bronchus, a harsh blowing sound is heard, which is conducted from the trachea; whereas, if a part of the lung free from large tubes, such as the apex or the base, be chosen, the sound is found to have diminished to a faint rustling, comparable to that produced by the soughing of the wind in distant trees—the *vesicular murmur* as it is called. Normally, it is only heard during inspiration and the commencement of expiration, and when it is more prolonged it is taken as an indication of some commencing abnormal condition. Its precise cause is not determined, some considering that it arises in the infundibula and air vesieles themselves, others that it is the tracheal or bronchial sound altered in transmission. When the lung is consolidated in disease, the eonsolidated tissue conducts the tracheal sound better than the normal healthy parenchyma of the organ, and over the consolidated areas the vesicular murmur is replaced by the latter.

Quantitative estimation of air respired.—The amount of air respired may be measured by the *spirometer*. This consists of a vessel inverted over water, the air being allowed to escape by a cock at the top, which is turned when the vessel is full. If air be expired through a tube leading into the vessel, which is balanced by weights like a

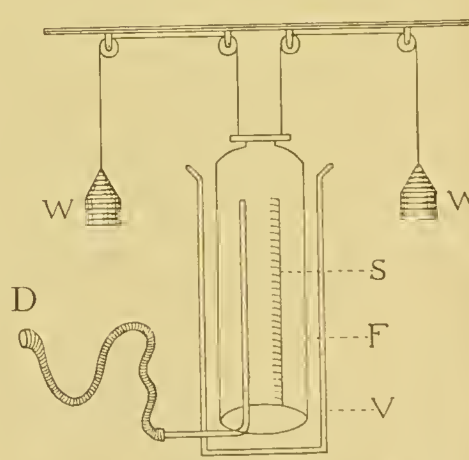

Fig. 225.—Scheme of Spirometer.

V, Vessel containing water; *F*, glass cylinder, with scale *S*, swung on pulleys and balanced by the weights *W*; *D*, breathing tube.

gasometer, some of the water is displaced, and the amount so displaced may be read off upon a scale, care being taken that the water within and without the vessel is at the same level, so that the pressure may be that of the atmosphere. Similarly, if the spirometer contain air and an inspiration be taken from the tube leading into it, the water rises to take the place of the air removed and the amount that has entered can be read off on the scale, with the same precaution as before.

The quantity of air taken in and given out during quiet respiration is about 20 cubic inches and this is called the *tidal air;* after this an additional 100 cubic inches may be taken in by the deepest possible inspiration, and this is termed the *complemental air;* and, similarly, after an ordinary expiration 100 cubic inches of air may be forcibly expired—the *supplemental air*—leaving still in the lungs 100 cubic inches of *residual air.*

If a deep inspiration be taken, followed by a forced expiration, it is obvious that the sum of the tidal, complemental, and supplemental air will be expelled, and this will amount to 220 cubic inches, according to the above figures. Roughly speaking, it varies from 225 to 250 cubic inches and has been termed, rather unfortunately, the *vital capacity.*

The tidal air (20 cubic inches) will thus be seen to form only a small part of the air in the lungs, and hence the alveoli are not exposed to direct changes in the air they contain but to those of diffusion, the oxygen passing downwards and the CO_2 upwards.

Nerve Mechanism of Respiration.

The respiratory movements are controlled by a centre which, like the vasomotor one, is bilateral and situated in the medulla. The two sides of the centre act in co-ordination with each other, and are situated rather higher than the vasomotor centre, corresponding very nearly in position with the vagus centres. It is connected, as the cardiac and vaso-motor centres have been seen to be, with both afferent and efferent fibres. The **efferent** are found in the nerves supplying the muscles concerned in the respiratory movements, which, for ordinary breathing, comprise the *phrenics* to the diaphragm and the *intercostal nerves* to the corresponding muscles and the levatores costarum, the fibres in these nerves being connected, from below upwards, first with nerve cells in the spinal cord and then with cells in the medullary centre. In extraordinary respiratory efforts of inspiration or expiration the efferent fibres are found in the motor nerves to the muscles enumerated in the list previously given.

The phrenic nerves arise from the third and fourth cervical, receiving also a branch from the fifth, and if the cord be divided below this point the diaphragm still remains in action, but the intercostal muscles are paralysed. Life, however, can be maintained by the continuation of the respiration through the medium of the diaphragm and the abdominal muscles.

If both phrenics are cut, on the other hand, the diaphragm is paralysed, and though the thoracic muscles still act they are insufficient in effectiveness to maintain life for any length of time. If one phrenic be cut, only the half of the diaphragm supplied by it is paralysed.

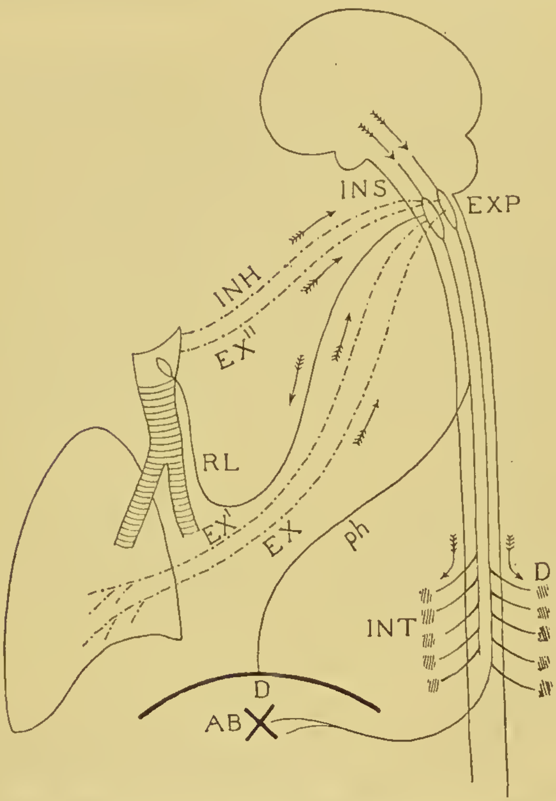

Fig. 226.—Diagram of Respiratory Nerves.

INS, Inspiratory, and *EXP*, expiratory centre. Efferent or motor nerves are represented by uninterrupted lines. *AB*, Expiratory motor nerves to abdominal muscles; *DO*, to muscles of back; *ph*, phrenic nerve to diaphragm *D*; *INT*. intercostal nerves; *RL*, recurrent laryngeal; *EX*. pulmonary fibres of vagus exciting expiratory centre; *EX'*, fibres exciting inspiratory centre; *EX''*, fibres of superior laryngeal exciting expiratory centre; *INH*, fibres of superior laryngeal inhibiting the inspiratory centre.

Thirdly, if the spinal cord be cut above the origin of the phrenic nerves, both the intercostal muscles and the diaphragm are paralysed and death results immediately. A modification of this last experiment reveals the interesting fact that the nuclei of the phrenic nerves in the two halves of the spinal cord are in intimate relation with each other across the middle line, for if one half of the cord be cut above the point of origin of the nerves, as we should expect the corresponding half of the diaphragm is paralysed; but if now the nerve itself on the *opposite* side be divided, the descending impulses from the

medulla, shut off from the chance of reaching the muscles on that side, cross over from one nucleus to the other, and so reach the half of the diaphragm which was previously paralysed, though the cord is divided on that side above the point of issuance of the nerve.

Such is, briefly, the relation of the respiratory centre to its efferent or motor fibres. Its **afferent** relations are not quite so simple and are intimately bound up with the general question of its automatic and reflex activity.

The inspiratory centre acts both automatically and reflexly, but under ordinary circumstances it depends for its rhythmical character on afferent impulses received from the lungs through the *vagus* nerve.* If one vagus be divided no very marked result follows, though the respiration becomes deeper and slower; but this result is much more pronounced if both the nerves are cut, death supervening in the rabbit in twenty-four hours, and in the dog in a week or more, preceded by pneumonia. One may conclude from the slowing of the respiration when the nerves are cut that the vagi, when intact, convey impulses to the medulla arising in their terminations in the pulmonary tissue, and we find that if the central end of the cut nerve be stimulated respiration quickens and finally the diaphragm comes to a standstill in the inspiratory position; but if the stimulus be weak respiration is slowed and the diaphragm comes to rest in the expiratory position; the latter being, also, the result when the *superior laryngeal* branch of the nerve—the sensory branch to the larynx—is stimulated.

From this experiment it may be concluded that two sets of fibres exist in the vagus, one of which conveys impulses to the medulla which stimulate the inspiratory part of the centre, and the other of which conveys impulses which similarly affect the expiratory part; or that one set of fibres exists which is differently affected by different forms of stimulation.

The question arises as to how the fibres of the vagus are normally stimulated and with alternating different results, *i.e.*, of inspiration and expiration; and this has been shown now, with a considerable measure of satisfactoriness, to be brought about by the alternate contraction and dilatation of the air vesicles of the lungs.

The evidence in favour of this view is as follows:—If air be pumped into the lungs so that the vesicles are repeatedly and forcibly distended, the contractions of the diaphragm become

* The vagus is also an efferent nerve in that it supplies the bronchial muscle fibres.

less, and the muscle finally stands still in the expiratory position. On the other hand, if air be pumped out of the lungs so that the air vesicles are repeatedly brought into a condition of partial collapse the diaphragm contracts more and more and finally comes to rest in the inspiratory position. From this it is concluded that distension of the air vesicles stimulates the ends of fibres in the vagus which carry impulses to excite the expiratory part of the centre in the medulla, while contraction or collapse of the vesicles stimulates the ends of fibres (perhaps the same) which excite the inspiratory part of the centre. And thus, in ordinary breathing — in the alternate distension and recoil of the walls of the air vesicles—we have in the rhythm itself the exciting cause of its maintenance.

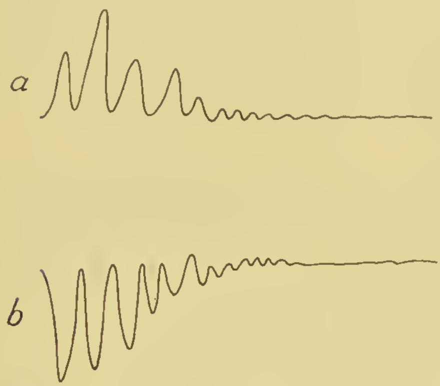

Fig. 227.—Tracings of Diaphragm. Upward Movements, Inspiration; Downward, Expiration.

a, Tracing from positive ventilation; *b*, tracing from negative ventilation.

As a corollary of the experiments it follows that if both inspiratory and expiratory efforts are made repeatedly and in excess of the normal, either voluntarily or experimentally, on an animal, respiration ceases for a time—a condition which is known as that of *apnœa.* At one time this was attributed to over oxygenation of the blood, which deprived the respiratory centre of the normal stimulus of venous blood flowing through it, and according to some (who considered the stimulation of the ends of the vagus to be affected by the chemical condition of the blood in the lungs) affected the terminations of the vagus in the same way. But this is disproved by the fact that the same condition of apnœa, or no breathing, results if the lung be ventilated with an inert gas, such as N or H, instead of air, though in this case the period of quiescence is shortened by the venosity of the blood stimulating the medullary centre. But the fact that, for however short a period, the condition of apnœa should ensue when hyper-oxygenation of the blood is excluded by the use of an inert gas shows conclusively that it cannot be regarded as the cause.

In addition to the afferent impulses reaching the centre by the vagus nerve we have to note that other impulses in the way of augmentation or inhibition reach it from the higher parts of the

brain. Thus the activity of the centre is to some extent under the control of the will and may be increased or diminished temporarily thereby. It is familiar to everyone that he can for a time breathe more quickly or slowly if he chooses, and also that he can for a minute or so refrain from breathing altogether; but at the end of this time the need for air becomes imperative and the excitation of the centre by the venous blood can no longer be controlled by the will. We have said that in the rhythm itself, inasmuch as it stimulates the terminations of the vagus in the manner already described, we have part of the mechanism for its maintenance, and it may be asked—How is it that when the vagi are cut the rhythm is still maintained, although the respirations are now slower and deeper? The explanation of this is to be found in the connection of the centre with the higher parts of the brain. As long as these connections are intact they can transmit impulses which appear to maintain the rhythmical character of the respiratory movements by their influence on the centre, even after the vagi are divided; and, on the other hand, the vagi alone can exercise this function after the higher paths are interrupted, though as before the respiration is deeper and slower; but when both influences are removed the centre passes into a condition of irregular excitement and quiescence and the animal soon dies.

In addition to the afferent impressions received through the vagus nerve and from the higher parts of the brain, the respiratory centre is frequently affected by stimulation of other nerves, giving rise to special respiratory acts, and some of these afferent nerves may now be mentioned. It will be obvious that they are not like the vagus constantly in action. The *superior laryngeal* branch of the vagus is the sensory nerve of the larynx, and when its peripheral terminations are stimulated by the presence of a foreign particle, *e.g.*, of mucus, a cough is the result, inspiration being inhibited, and a forcible expiration taking place against the obstruction of the previously closed glottis; the object of this action being—(1) To prevent the foreign body being drawn further down the respiratory tract, and (2) to expel it. A similar inhibition of the inspiratory part of the centre results from stimulation of the terminations of the *glosso-pharyngeal* nerve (the sensory nerve of the pharynx) during the act of swallowing, the object being to avoid the chance of the food being drawn into the larynx during its passage over its upper extremity (Fig. 224).

When a cough is produced intentionally with the object of clearing the throat rather than as the result of sudden stimulation of the superior laryngeal nerve, the forcible expiratory effort is

frequently preceded by a deep inspiration, which renders it more effective.

A cough may also be produced by stimulation of the terminations of the pulmonary branches of the vagus, as in consumptive cases, or even by irritation of the gastric branches of the nerve, as in the case of a "stomach cough." The application of cold to the skin may have the same effect, and thus the cutaneous nerves are another channel by which afferent impulses may reach the respiratory centre; an illustration of this being the quickening and deepening of the respiration on first entering the water on bathing.

The *nasal branch of the fifth* nerve when stimulated, as by a draught of cold air, gives rise reflexly to the special respiratory act known as *sneezing*, in which, however, the air is expelled not through the mouth but through the nasal passages, from which the offending matter is dislodged thereby; the force of the expiratory outblast being the greater if a previous deep inspiration be taken. If the bony part of the nose be compressed between the finger and thumb, a sneeze may often be cut short during its inception, the afferent impulses in some way being blocked, but how this occurs is not quite apparent, as the nerve to the mucous membrane does not lie between the skin and the bone. In the act of sneezing, however, we are not apparently limited to the mucous membrane of the nose as an exciting surface; a bright light is capable of acting as the exciting cause, the afferent nerve in this case being the optic. A respected relative of the writer had the faculty, of which he was no little proud, of inducing this special respiratory operation almost at will, by glancing at the sun with half closed eyes and head thrown back.

As we have had occasion in connection with the subject of the afferent impulses reaching the respiratory centre to mention these special respiratory acts of coughing and sneezing, it may be convenient to complete the list here. *Hiccough* is due to gastric irritation, *i.e.*, stimulation of vagus terminations in the stomach, and is caused by a sudden contraction of the diaphragm inducing an inspiration abruptly terminated by closure of the glottis. The condition is most readily relieved by holding the breath as long as possible, so as to break the habit of spasmodic contraction into which the diaphragm has temporarily fallen. *Sighing* and *yawning* are not the result of afferent impulses, but have a central origin in a condition of weariness or sorrow. They consist of a deep and prolonged inspiration, with a corresponding expiration, in the case of yawning, accompanied by movements of the muscles of the jaws and limbs. In *Cheyne-Stokes respiration*, which occurs in certain

nervous diseases, the respiratory acts are collected into groups, with pauses between them. It is not limited, however, to such cases, being observed to some extent in ordinary sleep. In some ways it is comparable with the variations in blood-pressure, known as Traube-Hering's curves, in the tracing (see "Vasomotor System").

We have thus seen that the respiratory centre in the medulla is, like the vasomotor and cardiac centres, also subject to the influence of impulses reaching it by various afferent nerves, but, in addition, it is very susceptible to the chemical condition of the blood passing through it, being powerfully excited by venous blood; and the question arises—Is this due to the presence of CO_2 or to the absence of oxygen? or if to both of these conditions, which has the most influence?

In the case of air in a limited space, which is respired again and again, the accumulation of CO_2 appears to be a potent factor in stimulating the centre. If an animal be compelled to breathe the same air again and again, as when its breathing space is limited, it is found that the breathing becomes exaggerated (hyperpnœa), then difficult (dyspnœa), and if the air remains still unchanged, asphyxia or suffocation results. The condition of hyperpnœa supervenes when the oxygen of the respired air falls from 21 per cent. (its normal proportion in the atmosphere) to 12 per cent. if the CO_2 is continuously removed by absorption with soda lime; nor does respiration become impossible until the proportion of oxygen falls below 6 per cent. Whereas if the CO_2 is not removed, marked hyperpnœa results when the proportion of oxygen has fallen only to 15·5, at which point the CO_2 present equals 5 per cent. In this case the hyperpnœa is clearly not due to the diminution of oxygen alone, but also to the concomitant presence of CO_2. The evidence generally on the subject shows that smaller variations in the amount of CO_2 than in that of the oxygen are sufficient to affect the centre.

The temperature of the blood also affects the activity of the centre. If the carotids be laid upon a closed receptacle through which a stream of hot water is maintained, a condition of "heat dyspnœa" results, whereas if the blood be cooled the respirations become slower and deeper.

We have now briefly referred to the action of afferent nerves, the influence of the venous state of the blood and of the temperature of the blood on the centre, and the question still remains as to whether it is capable of acting automatically, apart altogether from any of these influences. That the afferent impulses can be dispensed with, at all events for a time, is readily shown by section of the spinal cord below the bulb, and of the

vagus nerves. Respiration, in the ordinary sense of the word, then ceases, but the alæ nasi continue working, and as the venosity of the blood increases work more vigorously. But there seems no reason to suppose that the centre is automatic apart from the local conditions produced by the condition of the blood. It is true that in frogs breathing has been observed after removal of the heart, and also that in other animals, if the blood be replaced by normal saline, respiration can still go on. But in each of these cases is produced a condition (not the same in detail, but essentially the same so far as the centre is concerned) similar to that normally found in the case of the circulating blood, *i.e.*, the cells in the centre have not their need for oxygen satisfied, and the normal saline, or even the absence of any circulation at all, acts in this way in the same manner as venous blood. There is nothing in these experiments to prevent us supposing that the activity of the centre would fall into abeyance if it were not for the constantly recurring stimulus of the deficiency of oxygen in the blood-stream. Cutting off the blood-stream or replacing it with a neutral fluid is only another way of maintaining or even exaggerating the normal stimulus; and, a priori, we should expect that under these circumstances the respirations would, if anything, be increased rather than diminished, even if the centre was independent of any such stimulus.

Chemistry of Respiration.

The Chemistry of Respiration includes the gaseous interchanges (1) between the blood and the air of the pulmonary vesicles, and (2) between the blood and the tissues; the blood losing CO_2 and water vapour in the lungs and taking up oxygen, which it in turn hands over to the tissues in the capillary circulation generally, receiving carbon dioxide in its place.

The **gases of the blood** are *oxygen*, *carbon dioxide*, and *nitrogen* in much smaller amount. 100 volumes of arterial blood yield about 60 volumes of gas, containing 20 of oxygen, 40 of CO_2, and 1 or 2 of nitrogen; while the same quantity of venous blood yields 8 to 10 of oxygen, 46 of CO_2, and the same as before, 1 or 2, of nitrogen. The nitrogen is inert, and may be disregarded, but the oxygen and carbon dioxide are of prime physiological importance, and are for the most part held in weak chemical combination, only a small proportion of them being in simple solution. When placed in a vacuum blood "boils," giving up all its gas, and many "gas pumps" are in use for thus extracting the gases. The accompanying diagram of Pflüger's pump

will serve as an illustration of the principle common to them all. The bulb A is filled with blood by connecting the tube at its lower extremity with a blood-vessel, and the cocks 1 and 2 are then closed. The three-way tap 4 is first turned so as to connect D with G, a tube leading to a eudiometer F, which is not yet placed in position. E containing mercury is now raised, and the mercury consequently rises in D, driving the air along G. The tap 4 is now turned so as to connect D with C and B, and cut it off from G, and the mercury bulb E is lowered. The mercury therefore falls in D, and draws air from B through the drying tube C with it. The cock 4 is again turned so as to connect D with G and shut it off from B and C, the mercury bulb E is again raised, and the air withdrawn from B through C sent out by G. Tap 4 is now turned, the bulb E again lowered, and the process repeated until a sufficient approach to a vacuum in D is obtained, indicated by a manometer placed between C and 4.

The tap 2 is then opened, the gases bubble up through the blood and enter D. The eudiometer F filled with mercury is placed in position, tap 4 is turned as before to connect D with G and shut it off from C, the bulb E is raised and the mixture of gases forced into the eudiometer, the mercury in which it displaces. The process may be repeated until no more gas comes off from the blood. In this way 60 vols. of gas are obtained from 100 of blood, but we have yet to measure the relative quantities of the three. The carbon dioxide can be readily eliminated by the introduction of a little caustic potash, which absorbs it, the total volume of the gases being reduced to about one third. The amount of oxygen is similarly estimated by introducing sufficient hydrogen to combine with it to form water, when the mixture is exploded by means of an electric spark. Whatever reduction takes place in the total volume of gas so exploded one third of it is due to the oxygen. The remainder of the original mixture represents the nitrogen.

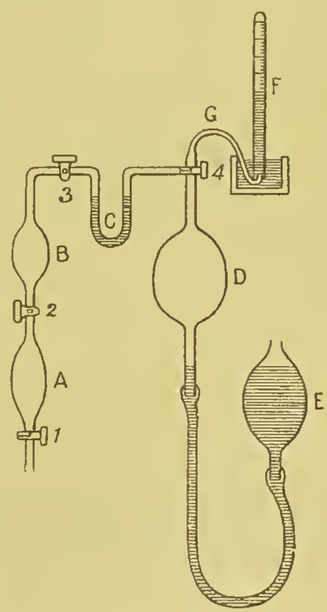

Fig. 228.—Scheme of Pflüger's Gas-Pump.

Hill's air pump (Fig. 229) is also simple and convenient. First the receiver R is raised and the whole apparatus thus filled with

mercury. a' is then closed and R lowered so that the blood-bulb, BB, is rendered a vacuum, a few drops of mercury being, however, left in it. The clip b is closed and the blood-bulb detached and weighed. Enough blood to fill about half one of the globes of BB is then introduced into it, by connecting the tube a' with a cannula placed in an animal's blood-vessel. The blood is defibrinated by shaking it with the mercury left in the bulb. BB is then weighed again to give the amount of blood, and reattached to the apparatus, hanging downwards as in the smaller drawing. The blood gases are then drawn off into d, which has been made a vacuum, and driven along e to the eudiometer E by raising R, the stop-cock c having been previously turned so as to cut off their passage back to BB. The gases can then be measured and analysed as before.

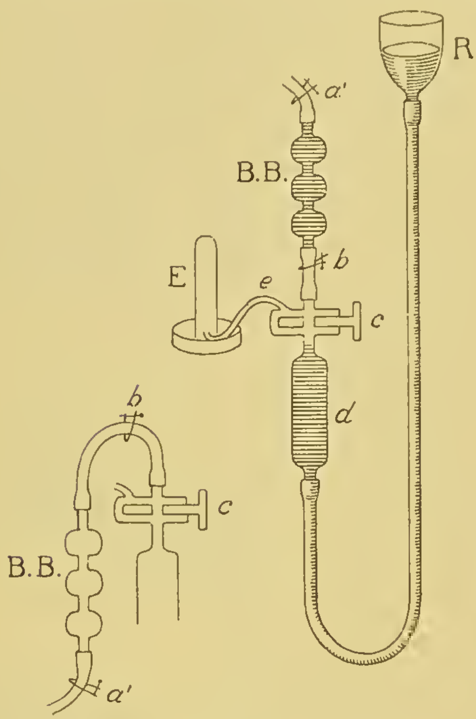

Fig. 229.—Hill's Air Pump.

B.B., Glass bulbs; a', clip on tubing; c, stop-cock with two ways to it, one from bulb d to *B.B.*, and the other from d to e, c may also be turned so that all communication between d and parts above is cut off; *R*, receiver connected with bulb d by stout tubing.

That the oxygen and carbon dioxide are present mainly as loose chemical compounds and not in solution alone is evident. The rule for the absorption of gases into solution by liquid is that the amount so absorbed varies with the pressure. But this is not the case with the gases of the blood. We find that when the gases are pumped from the blood in the manner already described very little oxygen comes off until the pressure is reduced to a certain level, when it is released with a burst as it were, the loose combination it has formed being overcome; and practically the same quantity of O is absorbed by the blood under varying pressures. Nor is the carbon dioxide merely in a state of solution. The quantity of a gas *absorbed* by a liquid is proportional to the

partial pressure of the gas; water at the pressure of one atmosphere will absorb and hold in solution about its own volume of CO_2. If the pressure be reduced to that of half an atmosphere it will hold half its volume, if to one-twentieth, one-twentieth of its volume. Blood-plasma, roughly speaking, will dissolve the same amount as water at the same pressure. But there is an important difference between them, in this, that when venous blood, which, as we have seen, contains 46% of its volume of the gas, is placed in an atmosphere containing only 5% of CO_2, this small percentage is found enough to keep the balance of things as it is—no CO_2 leaves the blood, and none enters it. It follows from this that the remaining 95 per cent. of the CO_2 is held not in solution but in chemical combination. Less than 1 volume of oxygen, and about 2 volumes of CO_2 (in 100 of blood) are in simple solution.

How are the oxygen and carbon dioxide combined in the blood? Nearly all the **oxygen** is united with the hæmoglobin of the corpuscles to form oxyhæmoglobin, in which it may be replaced, as we have seen, by such a gas as carbon monoxide. Very little of the oxygen is found in the plasma, and this is merely in solution and in passage between the air and the corpuscles in the alveoli of the lung, or between the corpuscles and the tissues in the rest of the capillary circulation. The corpuscles may in fact be regarded as reservoirs of oxygen, from which a constant supply is being given out to the tissues, and into which a constant supply flows from the air in the pulmonary alveoli, the two streams of income and expenditure being represented by the small amount found in solution in the plasma.

The interchange between the air and the plasma, and between the plasma and the tissues (or to speak more accurately the lymph which bathes them), depends on the common law for the diffusion of gases. The tension of the oxygen in the alveolar air being greater than that in the venous blood brought to the lungs, O passes from the air in the alveoli into the plasma of the blood circulating in their walls, and is immediately seized upon by the unsatisfied hæmoglobin of the corpuscles; whereas in the tissues, the tension of oxygen being higher in the plasma than in the lymph, a stream of oxygen leaves the blood for the latter, for the use of the tissue elements, and dissociation of oxygen from its combination with hæmoglobin in the corpuscles takes place to supply the place of the oxygen lost by the plasma. But the oxyhæmoglobin never becomes totally deoxygenated —the whole of the loosely combined oxygen is never parted with.

The **carbon dioxide** of the blood, like the oxygen, is for the most part in a state of loose combination, but the greater part of it is found in the plasma; all of it may be removed by a pump, but from plasma or serum (*i.e.*, blood from which the corpuscles have been withdrawn) only 95 per cent. can be thus extracted, the remaining 5 per cent. being fixed—*i.e.*, in firmer chemical combination. The whole of it comes off, however, on the addition of an acid, and from the experiment we conclude that in some way the presence of the corpuscles conduces to the liberation of the CO_2, perhaps by the oxyhæmoglobin itself acting as a weak acid. Most of the CO_2 is combined with sodium as the carbonate and bicarbonate, and a small part with phosphate of soda. The interchange of CO_2 between the blood and the air, and between the blood and the tissues, follows the same law as that of the oxygen, but here the order of things is reversed. The tension of CO_2 in venous blood is greater than the partial pressure of the same gas in the pulmonary alveoli, and hence it passes from the blood into the air; while the tension of the gas in the tissues is greater than that in the blood brought to them, and consequently CO_2 passes from the lymph into the plasma, where it is appropriated by the sodium to form carbonates. The following diagram will illustrate the diffusion of the O and CO_2 through the alveolar walls in the lung. The arrows indicate the direction in which the gas passes.

	CO_2	O	
Partial pressure of gas in alveoli of lung	27	27·44	
Alveolar membrane A	↑	↓	.... B
Tension of gas in venous blood of lung............	41	22	

Though we have thus explained the gaseous interchanges on the theory of diffusion alone, it would appear that the matter may be by no means so simple. It seems that the interchange in the lungs, as described above, of carbonic acid and oxygen can still take place when the partial pressure of the gases on each side of the alveolar membrane is equalised, and even when it is made unequal in the reverse of the usual direction. If this is so, it becomes necessary to suppose that the interchange is effected in part by the "vital activity" of the cells lining the alveoli, and is not therefore a process of mere diffusion; and, a

priori, we should be inclined to think that this would be the case, in view of the power of selection exhibited generally by animal cells, when these subtend some function of absorption or secretion. The swim-bladder of fishes also contains air, in which the amount of oxygen is greater than can be explained by mere diffusion alone.

Changes in the air during respiration.—Respired air has lost oxygen and gained carbon dioxide, water vapour, and putrescible organic matter, and its temperature is higher. The following table shows the comparative composition of Inspired and Expired Air :—

	Inspired Air.	Expired Air.
Oxygen	20·96 volumes per cent.	16·03 volumes per cent.
Nitrogen	79 „ „	79 „ „
Carbonic acid ...	0·04 „ „	4·4 „ „
Watery vapour ...	Variable.	Saturated.
Temperature......	„	36°C.

It will thus be seen that the loss of oxygen is 4·93, and the gain of CO_2 4·36 vols. per cent.; or, roughly speaking, 5 for oxygen and 4·5 for the CO_2. The difference in the composition of inspired and expired air may readily be ascertained by filling a burette with a sample of the air to be examined, and introducing substances which will absorb the gases. The amount of oxygen may be determined with pyrogallic acid, crystals of which are introduced under water and shaken up with the air in the burette. The difference in the level of the water in the burette before and after the experiment gives the amount of oxygen, but the levels must be read with the fluid at the same height inside and outside the tube. Similarly, by using caustic soda the CO_2 present is absorbed, and its amount is determined by the difference in the level of the water in the tube at atmospheric pressure before and after the experiment. The air of the room may be taken to represent inspired air, while a sample of expired air may be obtained by filling the spirometer with water and breathing into it a few times, avoiding, however, inspiring air from it. The burettes are then filled from the air in the spirometer.

The amount of watery vapour in expired air is estimated gravimetrically by passing it through a bulb of strong sulphuric acid,

when the increase in weight of the bulb gives the amount of water vapour in the air examined.

The amount of CO_2 and watery vapour excreted by an animal in a given time is estimated by enclosing it in a box through which air is drawn. After leaving the box the air passes through tubes containing (1) sulphuric acid, and (2) caustic potash. The difference in the weight of the first before and after the experiment gives the amount of water excreted; of the second the amount of CO_2. Fig. 230 shows the kind of apparatus required

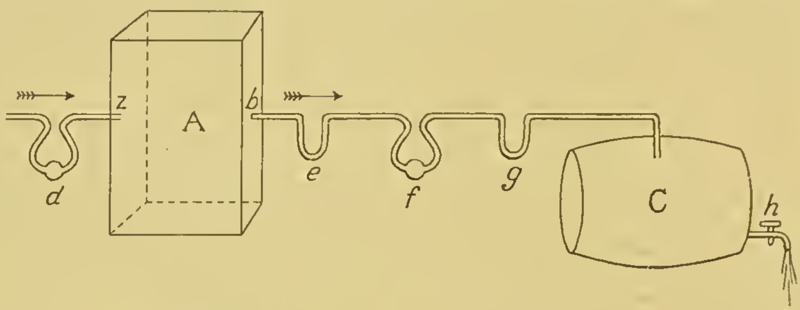

Fig. 230.—SCHARLING'S APPARATUS.

d, Caustic potash bulb to absorb carbonic acid from ingoing air; *A*, box containing animal; *e* and *g* contain sulphuric acid to absorb water; *f*, potash bulb to absorb CO_2 given off; *C*, vessel containing water; when the stop cock *h* is turned so that this runs off, air is drawn through the apparatus.

for such an experiment. *z* Represents the inlet to the chamber A, in which the animal is placed. *d* Contains caustic potash, so that the entering air is free from CO_2 to begin with; and a corresponding arrangement containing sulphuric acid for the absorption of water vapour, though not shown in the figure, should be placed on the entrance tube. The bend in the tube, *e*, also contains sulphuric acid, and the difference in its weight before and after the experiment indicates the amount of water vapour given off. *f* Contains caustic potash, and absorbs the CO_2, and like *e* is weighed before and after the experiment. *g* Contains, again, sulphuric acid to absorb water vapour which will come from *f*, and to estimate the weight of CO_2 *f* and *g* must be weighed together.

C is a chamber at first filled with water, and *h* a tap by which it can be run off and air consequently drawn in through *z*. This is Scharling's apparatus, but many others have been devised on the same principle, such as Regnault and Reiset's, Pettenkofer's and Haldane's.

As the air in respiration loses 5 of oxygen for $4\frac{1}{2}$ of CO_2, it follows that the total volume of expired air is less than that of inspired if the temperature and saturation with water vapour be

equal, for a molecule of oxygen (O_2) occupies the same space as one of carbon dioxide (CO_2) at the same temperature and pressure. The apparent loss of oxygen is due to the fact that it is not all used in the formation of CO_2, but some of it combines with hydrogen to form water, and some with the sulphur of the proteids. Upon a carbohydrate diet the loss of oxygen is less than on a meat one, for carbohydrates contain in themselves sufficient oxygen to oxidise their hydrogen to water. In a fat diet the loss of oxygen is greatest, because of the small amount of oxygen the fat contains—only one-sixth of what is needed for the oxidation of the hydrogen. The respiratory quotient is represented by

$$\frac{CO_2 \text{ excreted}}{O_2 \text{ absorbed}}.$$

and in man equals $\frac{9}{10}$, or ·9, if 5 be the amount of oxygen lost and $4\frac{1}{2}$ the amount of CO_2 gained. In the herbivora it may range from ·9 to 1, that is to say there may be no loss of oxygen at all, the CO_2 excreted exactly balancing the O absorbed.

A man weighing 70 kilos. gives off about 800 grammes of CO_2 and absorbs 700 grammes O in the 24 hours; with severe muscular exertion the amount of CO_2 may rise to 1300 grammes and the oxygen to 1100; while in rest the figures may sink to 700 and 600 grammes respectively. Other influences also determine the amount of CO_2 excreted. It is lower in females than in males. In the latter it increases up to the age of 30 and diminishes again after 50 is reached, in the former it diminishes after the climacteric. The more active the respiratory movements the more carbon dioxide is exhaled, but this must be distinguished from an increase in production. The taking of food increases it, while sleep diminishes it, from the absence of muscular exercise, light, and the taking of food. In hibernating animals much less of CO_2 is given off than is taken in of oxygen, so that the body weight is conserved as much as possible; the interchange between the air and the blood being carried out by diffusion and the cardio-pneumatic movements. Temperature has an important influence on the amount of CO_2 given off, and it acts differently on warm and cold blooded animals. The temperature of the latter varies with that of the surrounding medium, and hence if this is raised more CO_2 is given off, owing to the increased metabolism of the body generally, and *vice versa* if it is lowered; whereas that of warm blooded animals remains the same whatever the surrounding temperature may be, and if it be raised the metabolism (and

hence the excretion of CO_2) decreases to compensate for it, while if it be lowered the metabolism (and hence the excretion of CO_2) is increased (see "Animal Heat").

Breathing space required.—If the air in a room which is inhabited is not constantly renewed, in a varying time (depending on its size and the number of people in it) it becomes impure and cannot be breathed without inconvenience. As a matter of practical experience, it is found that air remains good as long as it contains no more than two parts of CO_2 in 10,000. Four parts in 10,000 makes the closeness of the room realisable, and it gets progressively more unpleasant till when nine parts of CO_2 are present it is unbearable, symptoms of headache, drowsiness and malaise supervening, and when such an atmosphere is breathed daily, anæmia and general debility result. These effects, however, are probably not produced by the CO_2 itself, which is a comparatively innocuous substance, but by the putrescible organic matter which accompanies it, as CO_2 added to pure air in similar quantity does not act in the same way. Though no definite body has yet been isolated from impure air capable of producing symptoms of poisoning of a similar kind, it is readily understandable that an impure atmosphere should disagree with air-breathing animals in the same way that dirty water does with fishes. It is to be noted that those who are subjected to the influence of impure air for the first time, such as students commencing to attend lectures, suffer most at first, and gradually attain a certain measure of immunity from the constitutional disturbances which first resulted from the often carefully closed windows of the lecture room—an immunity in many ways comparable to that obtained by innoculation; and it may very possibly be that the evil effect of such air has its cause in microbes or their products. As already stated for the reason given above, the CO_2 cannot be made responsible, nor is the effect due to deprivation of oxygen, for the blood will take up the usual amount of O from an atmosphere in which the percentage is more reduced than it is in such cases. That the excretions from the skin and the uncleanliness of the room itself, the furniture and the inhabitants, will contribute largely to the putrescent condition of the atmosphere goes without saying.

Though the CO_2 is not, therefore, the most deleterious element in a vitiated atmosphere, the amount of it is a very fair guide to its suitability or unsuitability for breathing purposes, for it goes hand in hand with the putrescible substances. If two parts of CO_2 in 10,000 is regarded as the permissible limit of impurity, each adult will require 3000 cubic feet of air per hour, at the end

of which time the CO_2 present will have reached that proportion, and the air will require to be renewed. In a sleeping room, each adult should have a space of 1000 cubic feet as a minimum, otherwise the air cannot be changed without giving rise to draughts.

Though the necessity of ventilation is obvious, it is a thing which is liable to be overdone under the apparent misconception that the oxygenation of the blood varies with the freshness or the reverse of the atmosphere; whereas between very considerable limits the amount of oxygen absorbed by the blood is the same and is independent of the partial pressure of the gas. That a little knowledge may be a dangerous thing is generally acknowledged, and the man who with "oxygenation" on his mind riddles the walls of his dwelling-house with the newest ventilators often exposes his family to risks from cold which far outweigh the advantages supposed to be derived from the constantly changing atmosphere. As a general rule, as long as the air of a room feels pleasant and not close it is fit for all the purposes of respiration; it is scarcely necessary to say that if it has any smell it should be changed at once.

If the air breathed be never changed, so that the vitiation proceeds indefinitely, *asphyxia*, or *suffocation*, ultimately ensues, and the same result is attained if oxygen in any other way is

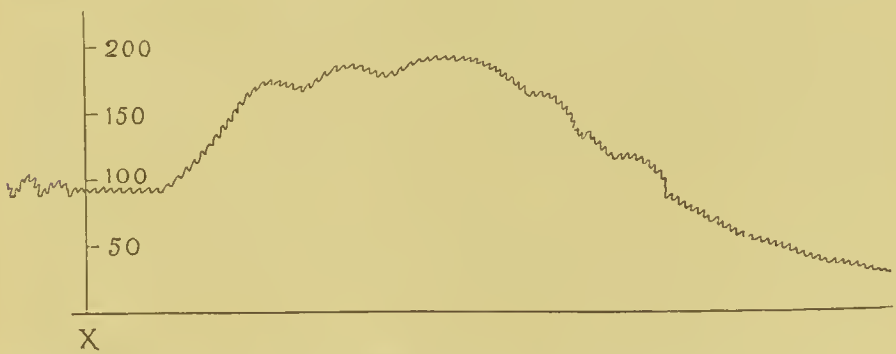

Fig. 231.—Curve of Blood-Pressure Tracing during Asphyxia (Reduced).
Artificial respiration stopped at *X*. Both vagi divided.

prevented from entering the blood; as, for instance, if the trachea be clamped, though then the onset of the condition is sudden and not gradual. The inhalation of an inert gas, such as nitrogen alone, or of one which will take the place of oxygen in its combination with hæmoglobin and form a more stable compound, such a gas as CO, has the same effect, and hence the somewhat familiar method of committing suicide by breathing charcoal

fumes. The symptoms of **asphyxia** may be divided roughly into three stages, though it must be remembered that these pass somewhat gradually into each other. The first evidence of the impending condition is hyperpnœa or exaggerated breathing, in which the respirations become more rapid and deeper, followed by dyspnœa, in which the breathing is carried on with obvious difficulty, the extraordinary muscles of inspiration being first brought into play, succeeded by all the expiratory muscles, as the result of stimulation of the centre in the medulla by the venous blood circulating through it. The second stage is characterised by the respiratory movements becoming convulsive, and the convulsions spreading to the muscles of the body generally. In both these stages the blood-pressure is greatly raised, being at its maximum in the second. The third stage is that of exhaustion accompanied with insensibility and the absence of the conjunctival reflux. The breathing is represented by sighing inspirations at longer and longer intervals, the blood-pressure is low and the pulse almost imperceptible, and finally with its absolute stoppage death ensues.

When the chest is opened post-mortem, the right side of the heart, the systemic veins near the heart, and the pulmonary artery are found engorged with dark venous blood, while the left ventricle, the systemic vessels, and the pulmonary veins are empty. The stages may be studied experimentally by opening the chest of a dog, placing a manometer in a branch of the pulmonary artery and another in a systemic vessel and watching the phases as they ensue when artificial respiration is discontinued. The course of events seems to be as follows :—When oxygen ceases to enter the blood it rapidly becomes venous, and thus stimulates the vasomotor centre (as well as the respiratory), leading to a general constriction of the peripheral arterioles, including those of the splanchnic area, and a consequent rise in the general blood-pressure, and distension of the left side of the heart. The pressure in the pulmonary artery, however, does not rise so much as elsewhere, perhaps due to its greater distensibility or to the vasomotor centre not exerting the same constricting influence on its arterioles. The left ventricle next becomes enfeebled from the venous blood supplied by the coronary arteries, and no longer able to contract against the increased peripheral resistance, so that it is brought almost to a standstill. In the meantime the vasomotor centre, at first stimulated by the venosity of the blood in turn becomes paralysed by it and loses its grip on the peripheral arterioles, which consequently dilate, the blood-pressure falling, and the ventricle commencing to beat again

feebly. The blood now accumulates in the right side of the heart, as the weakened right ventricle is unable to drive it through the pulmonary circulation, the engorgement being assisted (if the chest is unopened) by violent inspiratory efforts which diminish the intra-thoracic pressure.

We find, therefore, that in the earlier stages of asphyxia the left cavities of the heart and the systemic vessels are distended; in the later stages those of the right side, the systemic veins and pulmonary artery.

Recovery from asphyxia is rare after oxygen has been withheld for four or five minutes. In cases of drowning water may displace the air from the vesicles and prevent its re-entry, and a much shorter time may be fatal. The principle of most of the methods of resuscitation is to first ensure that the air passages are unobstructed, by the removal of any foreign substance, and then pursue artificial respiration. Coincident rhythmical compression of the heart is likely to be of service as it causes a slight movement of the blood, and at the same time acts as a stimulant to cardiac contraction. In Sylvester's method of treating cases, the patient is placed on his back, the tongue being drawn forward to ensure the free access of air to the trachea, and his arms are alternately placed in the extended position above his head (*i.e.*, in line with the body) so as to raise the chest and imitate the movement of inspiration, and depressed against the sides of the chest, on which slight pressure is made, to imitate expiration. A couple of seconds should be allowed to elapse between each movement, and the respiratory cycle should be repeated about 15 times per minute. As soon as spontaneous efforts at respiration are observable, the artificial respiration is stopped and steps taken to promote circulation and warmth.

Experimentally in the laboratory artificial respiration is effected by means of a bellows attached to a cannula tied into the trachea.

Effect of drugs and respiration of foreign gases.—These may act directly on the centre or indirectly by varying the amount of oxygen in the blood. Thus, as we have seen, carbon monoxide gas (CO) when respired produces asphyxia by uniting with the hæmoglobin of the red blood-corpuscles to the exclusion of the oxygen, of its supply of which the respiratory centre is thereby deprived; and hydrocyanic acid has a somewhat similar action.

Nitrous oxide or "laughing gas" and carbon dioxide (in considerable quantity, *e.g.*, 30%) act directly on the centre as narcotics. Alcohol at first stimulates the centre, then weakens it, and finally in still larger doses abolishes its activity altogether

before the heart itself is paralysed. Chloroform similarly paralyses first the respiratory, and then the cardiac centre, but it must be borne in mind (in relation to the administration of the vapour in surgery) that cardiac failure may result indirectly from paralysis of the vasomotor cells presiding over the splanchnic area, and a consequent fall in blood-pressure, sufficient to cause failure of the heart's action from the withdrawal of blood from the organ itself and the brain.

Effect of changes in the barometric pressure.—Ordinarily the pressure of oxygen respired is one-fifth of the atmosphere (atmospheric pressure = 760 mm. mercury), that is to say, it is proportional to the percentage amount of oxygen in the air; but respiration can still be maintained when the pressure is reduced by one half, as it often is at considerable altitudes. If the pressure be still further reduced to less than 7 per cent. oxygen pressure, asphyxia ensues, preceded by bleeding from the nose and alterations in the blood-pressure. The pressure of the air respired may be considerably increased, too, without increasing the amount of oxygen in the blood, which remains the same at any pressure between two-and-a-half and one-half an atmosphere. But a pressure of three atmospheres of pure oxygen (or 15 of air) is sufficient, according to the experiments of Bert, to induce tetanic convulsions; the amount of oxygen absorbed and CO_2 excreted being both diminished; and these experiments thus afford still further evidence that the gaseous interchange between the air and the blood is not a matter of diffusion alone. In this connection it may be mentioned that when an animal breathes a completely indifferent gas, such as N, H, or CH_4, its blood yields no oxygen to it.

The **influence of respiration on the blood-pressure.**—We have seen that in a blood-pressure tracing, such a one as may be obtained by means of a mercurial manometer placed in connection with the carotid artery, certain oscillations which are called "respiratory waves" occur; and we have now to consider the way in which these variations in the mean pressure are produced. If a tracing of the respiratory movements of the chest wall be recorded synchronously with one of the blood-pressure, it is found that, generally speaking, during inspiration the pressure rises and during expiration it falls; but to be more precise, the rise and fall in the blood-pressure does not exactly correspond with the two phases of respiration, but in each case is a little behind time. In other words, the maximum of inspiration is attained before

the highest level of the blood-pressure is reached, and the minimum of expiration before the lowest level; the blood-pressure continuing to rise for a short space after inspiration is at an end, and to fall after expiration has ceased and inspiration recommenced. For the moment, however, we may neglect this discrepancy and regard the rise of pressure as occurring *pari passu* with inspiration and the fall with expiration.

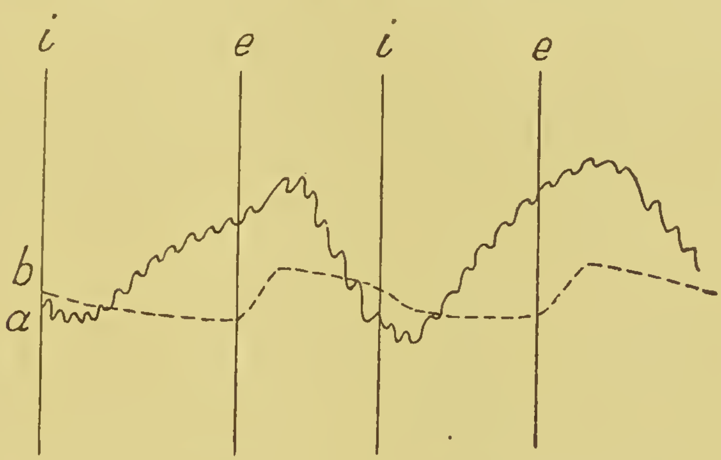

Fig. 232.—Blood-Pressure Curve and Curve of Intrathoracic Pressure.

a, Curve of blood-pressure; *b*, curve of intrathoracic pressure; *i*, inspiration, commencement of; *e*, expiration, commencement of.

The influence of respiration in producing this oscillation might be (1) *mechanical, i.e.*, dependent on the pressure conditions in the thoracic cavity resulting from the alternate increase and decrease in the capacity of the chest, or (2) *nervous, i.e.*, dependent on an effect upon the circulatory system, produced through the medullary centres; and both theories have found supporters. That the heart is to some extent affected during respiration is evidenced by the fact that the number of beats is greater during inspiration than expiration, and it might be supposed that its greater rapidity of action led to the rise in pressure, as we know it to be capable of doing. But on the other hand, the fact that the oscillations in the blood-pressure are still present, even after the vagi are divided, shows that the recurring stimulation of the cardio-inhibiting centre, which is the cause of the slowing of the beat during expiration, cannot be held responsible for the respiratory curves. Traube-Hering's curves, which occur during the later stages of asphyxia, are undoubtedly due to nervous influence—to rhythmical discharges from the vasomotor centre; but they are of greater length than

the ordinary respiratory oscillations, which may sometimes be seen superimposed upon them. We can only regard Traube-Hering's curves therefore as evidence that the vasomotor centre is capable of sending out rhythmical impulses which produce curves on the blood-pressure tracing somewhat similar to those of ordinary respiration, but we must recognise that these curves are not identical with them.

The more generally accepted view of the cause of the respiratory undulations is that these are due mainly to the changes of pressure resulting from the periodic movements of the chest wall. When inspiration takes place the intrathoracic pressure (always less than that of the atmosphere except when forced expiratory efforts are made with the exit from the air passages closed) is decreased and blood is drawn into the large veins in the chest, and thence into the right side of the heart; and this leads to a general advance in the progress of the blood towards the systemic tree, for it is at once sent from the right side of the heart through the lungs into the pulmonary veins, and thence through the left side of the heart into the aorta; its passage through the lungs being facilitated by a decrease in resistance in the pulmonary capillaries, which accompanies expansion of these organs. Thus during inspiration the pressure in the aorta and systemic tree generally is raised, from the accession of blood into it from the right side of the heart. Expiration has exactly the opposite effect, for the increase in the thoracic pressure which then takes place hinders the entrance of blood from the venæ cavæ to the right side of the heart, and the collapse of the lungs increases the resistance to the passage of blood through them to the aorta.

We may now ask—Why is it that the respiratory undulations of the blood-pressure curve do not exactly correspond with the respiratory curves obtained by means of the stethograph? Why does the blood-pressure for a short period still maintain itself, and even reach its maximum a little after inspiration has ceased and expiration begun? The answer to this seems to be found in the fact that a brief period must be allowed for the new condition of affairs to assert itself—to overcome as it were the inertia of the preceding state. When expiration commences, the dilated lungs contain an excess of blood, and as they collapse this is driven by their decreased capacity for holding it into the aorta, and so maintains the pressure for a short time. This effect is of course but momentary, and quickly over-borne by the more important influence of the increased resistance in the capillaries of the lung which attends their collapse, but its existence, even for a brief

space, will delay the fall in pressure. Similarly, too, in inspiration the lungs must first be filled with blood to the extent of their increased capacity before the diminished resistance in their capillaries can effect the pressure in the aorta. Another cause of delay is to be found in the fact that the aorta is affected by inspiration and expiration in a similar way to the venæ cavæ, though to a less extent. Thus the first effect of inspiration upon the aorta is to draw blood into it from the systemic tree; and though on account of the thickness and rigidity of its walls this effect is small and is quickly neutralised and overcome by the much greater influence in the opposite direction of the indraught of blood through the veins to the right side of the heart and the decreased resistance in the lungs, it is sufficient to account for some of the delay.

Inner or Tissue Respiration.

By "internal respiration" is meant the interchange of gases (CO_2 and O) between the tissues and the blood, the former taking up oxygen and giving out carbonic acid. That the lungs themselves are not the seat of the oxidation processes (beyond in so far as they themselves are tissues) is evidenced by the fact that carbon dioxide is found in greater amount in the blood going to them than in that leaving them, and the temperature also is no higher than elsewhere. Neither is the blood the main seat of the processes, for if the blood of a frog be replaced by normal saline and the animal kept in an atmosphere of pure oxygen, carbonic acid gas is still given off; and necessarily in this case the CO_2 must come from the tissues themselves. The avidity of the tissues for oxygen is shown by the fact that if methylene blue be injected into the circulation and the animal killed shortly afterwards, the organs are found at first colourless, but rapidly become blue on exposure to the air; the reagent having been rendered colourless by reduction in the first instance, and then recovering its oxygen on exposure after death. The liver, kidney and lungs exhibit a special affinity for oxygen and are particularly active in reducing such pigments, the pancreas and submaxillary gland being much less active in this way.

Another indication of the tissues being the source of the CO_2 given off from the lungs is afforded by the presence of the gas in the lymph with which the tissues are bathed, or in the lymph coming from them and in the tissues themselves; muscle, which we may regard as a typical example of a respiratory tissue, yielding when "pumped" a considerable amount of CO_2 but no oxygen.

It is a noticeable feature in the respiration of muscle that CO_2 continues to be produced by it in an oxygen-free atmosphere, in which too it can do a considerable amount of work, showing that the CO_2 is not the result of an immediate union of the oxygen absorbed with carbon, but that the oxygen so absorbed is stored up in the form of some compound (or compounds) which breaks down during muscular contraction, CO_2 being liberated. So that here we have a marked difference between tissue respiration and ordinary combustion.

The amount of CO_2 given off by an excised mammalian muscle is markedly affected by its temperature and state of activity. If the temperature is raised, less CO_2 is given off; and when it is lowered, more; the respiratory quotient being thus in the former case reduced and in the latter increased. When stimulated to contraction more CO_2 is given off and more O absorbed than when the muscle is at rest, the increased consumption of oxygen being the more marked.

The activity of tissue respiration is greatest in muscle and nerve-cells and other forms of energising protoplasm.

CHAPTER VIII.

ALIMENTATION.

WE have considered the means whereby the blood receives its supply of oxygen, and now pass to the consideration of the food supply proper, and the changes it undergoes in the alimentary canal before absorption into the blood-stream. In a subsequent chapter we shall deal with absorption itself, and later with the excretion of the end products of the food from the organism. The changes which the food undergoes in the tissues themselves (metabolism), though naturally following absorption, is more conveniently dealt with after the excretion of the end products has been considered.

The alimentary canal commences at the mouth and terminates at the anus, and its main functions are those of *digestion* and *absorption*, these processes being mechanically aided by mastication, deglutition, &c. By the digestive action of the juices poured out at various points in its course such food stuffs as natural proteids and starch are rendered soluble, so that they readily pass through the epithelial layer lining it and enter the blood-stream, and fat is more finely divided previous to its passage through the epithelium and absorption by the lymphatics. The salts, water and dextrose of the food are absorbed unchanged. The various food stuffs we shall consider later in greater detail: at present it will be enough to say that they include proteids, carbohydrates, fats, salts and water, and that a mixed diet including representatives of all these classes of substances is required by man; it being noted, however, that it does not follow from this that any constituent of the tissues must necessarily be derived from one belonging to the same series in the food. But of this we shall have to speak more fully later, when the subject of metabolism is under consideration.

The alimentary canal is a muscular tube of considerable length, lined with epithelium, which is secretory or absorptive in the greater part of its extent. But, in addition to this, at certain points special "exvaginations" of the epithelial layer have taken place to form the large glands which add their

secretion to that of the wall of the alimentary canal itself. Thus opening by means of their ducts into the mouth we have the submaxillary, sublingual and parotid glands—the "salivary glands" as they are termed; and into the duodenum the liver and pancreas pour their secretion by a duct common to both. It may be of advantage to consider in a general way how such glands are developed, their more particular and individual characters being reserved till their secretory function is dealt with.

Secretory epithelium in its simplest form consists of a single layer of cells resting upon a substratum of connective tissue in which blood-capillaries ramify, and the function of the cells is to withdraw from the lymph of the connective tissue the substances required for its secretion—these being of course supplied by the blood in the capillaries. An example of such a simple secretory epithelium is to be found in the pleura of the lung or any other serous sac. But this is an instance of the simplest of all secretory apparatus, and when the secretion is more specialised, as it is in the case of the alimentary glands, a more complicated arrangement of the epithelium is found. The first step towards the more highly organised glands is represented by an inpushing of the epithelium in a saccular or tubular form into the connective tissue beneath it, and such an inpushing is termed a *simple saccular* or *tubular gland*, and the economy in space resulting from such a modification of the most simple type is obvious. Of simple tubular glands, *Lieberkühn's follicles* of the intestine are examples, while the skin of the frog affords instances of the simple saccular variety. But though an increased area for the epithelium is thus obtained by the dipping down of the tube or saccule, as the case may be, into the connective tissue beneath it, and though this is by far the most common way in which the glandular surface is multiplied, it must not be overlooked that out-growth as well as in-growth will serve the same purpose, and that such a method in a simple degree of development is adopted in the case of the synovial fringes in joints.

The cells lining the tubules or saccules are columnar or cubical, and belong now to the category of glandular epithelium. When a further stage of development is reached the tube or saccule is found divided into two or more in the lower part, the portion above, opening on the surface, remaining as their common duct, through which the secretion escapes. Such compound tubular glands are to be found lining the wall of the stomach, the lower divided portion being secretory and the upper undivided part the duct. Brunner's glands in the wall of the

duodenum are also compound, but their ducts are much longer. Thus the glands lining the stomach and intestine are of a comparatively simple kind, being either in the form of simple tubes (Lieberkühn's follicles) or tubes which are divided once or twice at their lower ends (gastric and Brunner's glands). The large glands, such as the salivary glands, the liver and pancreas, however, show a much greater complexity of structure, though the difference is merely one of degree and not of kind. In the case of these glands the duct divides again and again before the terminal secretory part of the gland is reached, the whole arrangement in the salivary glands reminding one somewhat of a bunch of grapes; the grapes themselves representing

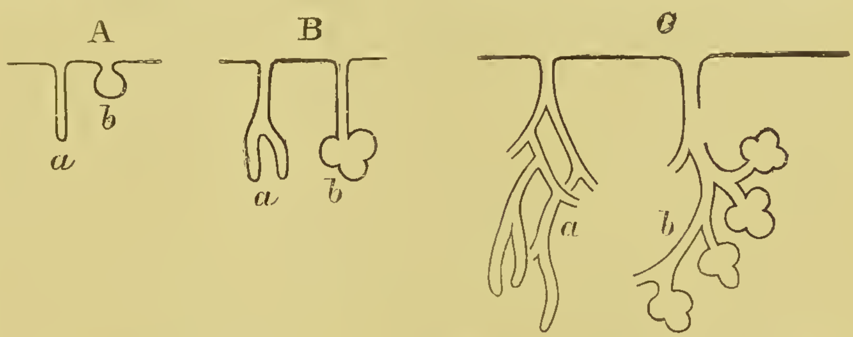

Fig. 233.—Diagram of Different Classes of Glands.

A, Simple; *B*, commencing complexity; *C*, compound; *a*, tubular; *b*, saccular.

the *acini* or terminal secretory portion, and the stalks the ducts. Between the acini is the supporting connective tissue of the organ, containing a capillary network. This connective tissue is usually so arranged that laminæ of it split the gland as a whole into lobes, and these again into lobules; it also affords a general fibrous investment to the gland.

We shall now pass to the consideration of the structure and function of the different parts of the alimentary canal in their relation to the digestion and absorption of food, commencing with the study of the changes it undergoes in the mouth.

Insalivation.

The buccal **saliva** is a mixture of the secretion of the small mucous and serous glands found beneath the stratified squamous epithelium lining the mouth and that of the large and more important salivary glands proper—the parotid, submaxillary and sublingual. It is a glairy, opalescent, viscid fluid, of slightly

alkaline reaction, and a specific gravity of 1002 to 1006. On microscopical examination, epithelial plates detached from the epithelium of the mouth, "salivary corpuscles" from the salivary glands, and leucocytes or lymph cells from the tonsils may be seen in it; their presence being rather accidental to the cavity into which the saliva is poured than of any physiological significance. The chemical constituents of mixed saliva are the following:—(1) *Organic*: mucin, serum albumin and globulin, and ptyalin; (2) *inorganic*: sodium chloride, sodium carbonate, magnesium phosphate, calcium phosphate and carbonate, and potassium sulphocyanate.

The viscidity of the saliva is due to the presence of mucin, which is far the most abundant of the organic substances, and is separable as a ropy mass on the addition of acetic acid. Saliva becomes cloudy on standing, due to a precipitation of the calcium carbonate, when the CO_2 which held it in solution escapes; and in a similar way the carbonate and phosphate of calcium sometimes becomes deposited on the teeth as tartar. It assists in articulation by moistening the mouth—speech being rendered almost impossible if the secretion is stopped, as by emotion: and by its power of dissolving sapid substances, and so bringing them into relation with the terminations of the gustatory nerve, it subserves the function of taste: it also moistens the food in mastication, and lubricates the passage of the bolus in deglutition. These are its more mechanical functions: its *digestive* action depends on the presence of the ferment *ptyalin*, which by its *amylolytic* action upon starch, converts it into a reducing sugar—maltose. Sometimes the action is called *diastatic*, because it is similar to that of *diastase* in germinating grain. In some animals, however, the saliva has no digestive action.

The starch upon which the saliva thus acts belongs to the group of substances known as carbohydrates, which may be arranged roughly in three subdivisions:—

(1) The starches or amyloses, including starch, glycogen, and dextrin. Starch has the formula $(C_6H_{10}O_5)n$, and is the anhydride of glucose, thus:

$$C_6H_{12}O_6 - H_2O = C_6H_{10}O_5.$$

(2) The glucoses, including dextrose (glucose), levulose and galactose, have an empirical formula $C_6H_{12}O_6$, and may be regarded as the aldehydes or ketones of hexatomic alcohols $C_6H_8(OH)_6$.

(3) The saccharoses, including cane-sugar, lactose, and maltose, may be regarded as composed of two molecules of glucose minus one of water, thus:

$$C_6H_{12}O_6 + C_6H_{12}O_6 - H_2O = C_{12}H_{22}O_{11}.$$

We have previously considered the characters of these substances, and need only now deal with them in relation to salivary digestion. When saliva is added to a solution of boiled* starch at a suitable temperature—the most favourable is that of the body, *i.e.*, 37°C.—and allowed to act upon it for a few minutes, it first loses its opalescence and is converted to *soluble starch*, which still gives the usual blue reaction with iodine. But this reaction is quickly superseded by the appearance of red colouration on the addition of the same reagent, due to the presence of *erythrodextrin*, and this in its turn is followed by an absence of any reaction at all, the erythrodextrin being by this time converted to *maltose*. The conversion to maltose is thus not a direct change, there being apparently several intermediate stages, nor does the whole of the starch ultimately undergo this change, some of it remaining to the end as dextrin (*achroodextrin*), and a small part being converted to *dextrose*.

The following equation may perhaps help to the understanding of the change to dextrins.

$$\underset{\text{Starch.}}{10(C_6H_{10}O_5)n} + \underset{\text{Water.}}{4n(H_2O)} =$$

$$\underset{\text{Maltose.}}{4nC_{12}H_{22}O_{11}} + \underset{\text{Achroodextrin.}}{(C_6H_{10}O_5)n} + \underset{\text{Erythrodextrin.}}{(C_6H_{10}O_5)n.}$$

As soon as the maltose is formed, its presence is readily detected by boiling the mixture with Fehling's solution, when the copper oxide is reduced. Of the two dextrins, erythrodextrin only appears temporarily. As we have just said, some of the dextrin remains to the end in artificial digestion, and the quantity so left varies according to whether the sugar is dialysed away as it forms or not. That is to say, that in the presence of an excess of its product—sugar—the action of the ptyalin becomes progressively less, and the amount of unchanged dextrin greater; if the sugar be removed by dialysis as it is formed, a much smaller percentage of the starch is found at the end in the form of dextrin, as the action of the ptyalin continues vigorously. What is the nature of the substance ptyalin? There seems no doubt but that it belongs to the class of unorganised ferments. It is present in extremely small quantity, and like the ferments generally does not seem to be used up in the process of its action. It is also subject to temperature conditions, the most favourable being that of the body, its activity decreasing as this is lowered; though the conversion of starch to sugar will still go on at the temperature

* If the starch is unboiled, the cellulose envelopes of the starch granules protect the contained granulose from the action of the ptyalin, which is thus much delayed.

of the atmosphere. On boiling, the saliva or solution of ptyalin loses its amylolytic power, nor does it recover it on cooling. Furthermore, its action is "hydrolytic," and this is characteristic of ferments generally. It acts best in a neutral medium or a slightly alkaline one; the presence of ·1 per cent. of hydrochloric acid will arrest its activity altogether.

If filtered saliva be treated with an excess of alcohol (15 to 20 times its bulk), all the proteid matters are precipitated just as they are when blood-serum is treated in a similar way. If after some days, when the proteids have become coagulated, a watery extract be made of the precipitate, the ordinary proteids remain undissolved, but the ptyalin passes into solution and the extract has the same power of converting starch to maltose as saliva itself; but the active substance exists in so small an amount that it has not been further isolated. An aqueous infusion of a ptyalin-producing gland also possesses the digestive properties of saliva; and if a fresh gland be minced and treated with an excess of alcohol in the same way as the saliva itself, described above, a glycerine extract, prepared by covering the coagulated portions of the gland with glycerine after the alcohol has been removed, is very active.

Structure of the salivary glands.—The parotid, submaxillary, and sublingual are compound tubular glands of a racemose type, that is to say, the subdivisions of their ducts and the tubules, or alveoli in which they terminate, have a general resemblance in their arrangement to a bunch of grapes. The cells of the alveoli are the secretory part of the gland and differ in character totally from those lining the ducts. They are comparatively large nucleated cells in a single layer and nearly fill the space occupied by the alveolus to which they belong, only a small lumen being left; and this, under certain circumstances (*i.e.*, if the gland has been resting and its cells accumulating within them the precursors of secretion), may be so small as to be unrecognisable as such. In shape the cells are necessarily somewhat like a wedge, the conical end being directed to the lumen (actual or potential) and the broader base resting on the membrane surrounding the alveolus. This basement membrane consists of a single layer of flattened connective tissue cells, an imperfect layer which is continued in a still less perfect form along the ducts. Between the alveoli, outside the basement membrane, is a small amount of connective tissue supporting a capillary network, lymphatics, and nerves.

The subdivisions of the ducts are lined for the most part by a layer of vertically-placed columnar cells, each of which contains

an oval nucleus, the cell substance itself being vertically striated in its outer part. In the larger branches of the ducts this columnar epithelium becomes stratified, and the connective tissue immediately outside it is arranged in the form of a distinct sheath, in which circular muscular fibres of the non-striped variety appear as the main duct is approached. The smallest ducts may each terminate in one alveolus alone, or in two, three or more, which thus open into a common lumen (Fig. 234). At the point where the duct joins the alveoli, or a little before it, its epithelium becomes changed in character to "low cubical," as it is sometimes called, or even to squamous; and this part of the tube (usually very short) is termed the *intermediate duct* or *ductule* (Fig 234, *b*).

Fig. 234.—Section of Submaxillary Gland of Dog.

a, Interlobular duct, ending in *b*, intermediate duct; *c*, alveolus showing lumen; *d*, alveolus cut excentrically; *e*, connective tissue between alveoli; *f*, parietal cell (demilune); *g*, central mucous cell; *h*, nucleus of basement membrane cell.

The gland as a whole is surrounded with a capsule of connective tissue, which sends in septa, separating its substance into lobes or larger lobules—the *interlobar septa* or trabeculæ; and from these are given off in turn finer plates, still further dividing the substance of the gland—the *interlobular septa;* and these in turn break up into still finer subdivisions of connective tissue, which penetrate the lobules themselves, and are continued as the connective tissue between the alveoli already referred to—the *intralobular connective tissue.* The large ducts and vessels run in the interlobar and interlobular tissue, the smaller ones and ductules between the alveoli themselves; the ducts being conveniently named from the position in which they occur—interlobar, interlobular, and intralobular. The main duct of the gland, formed by the confluence of all its subdivisions, is of considerable length, so that the secretory portion (as contrasted with simple glands) is removed a considerable distance from the epithelium of the mouth, on the surface of which its secretion is poured.

As far as the general arrangement of their parts is concerned the above description will apply to each of the three salivary glands, and in the more intimate structure of their ducts no distinction worth comment is to be observed. They differ, however, considerably from each other in the character of their secretory epithelium, and this is accompanied with a corresponding difference in the quality of their contribution to the mixed saliva of the mouth. Thus the secretion of the parotid is thin and serous, and contains ptyalin but no mucin, and it is hence termed a *serous* gland; that of the sublingual is markedly mucinous and viscid, and contains no ptyalin, and it is a purely *mucous* gland; that of the submaxillary is less viscid than the sublingual secretion, but contains mucin, so that it is mucous; and, like the parotid saliva, it also contains ptyalin. In fact, in the structure of its alveoli and the nature of its secretion it partakes of the character of both the parotid and sublingual glands, and hence is a *muco-serous* salivary gland.

We have now to study the anatomical features underlying this difference in the secretion of the three glands.

When the alveoli of the **parotid**, which is a true salivary gland (all its alveoli producing the distinctive amylolytic ferment), are examined under a higher power of the microscope they are seen to be somewhat quadrangular or polygonal in outline, from mutual pressure, with the corners rounded, and lined by a layer of granular cells surrounding a lumen, which is generally distinguishable merely as a point or line. The cells stain somewhat deeply as a rule with the reagent, and their rounded nuclei are placed about their centre or a little to the outer side of it. The appearance of the cells, however, and consequently of the alveoli which they compose, varies somewhat with the functional activity of the gland, though this difference is not so marked as in the case of mucous alveoli, to which we shall presently refer. If the cell be resting and loaded with granules of the precursor of secretion, which stain less deeply than the protoplasm in which they lie, it appears as a whole to be less deeply stained, it is increased in

Fig. 235.—Changes in the Parotid during Secretion (diagrammatic). (Langley.)

A, During rest; *B*, after moderate stimulation; *C*, after prolonged stimulation.

size, and its nucleus is somewhat obscured. After secretion the cells are smaller, a lumen may become discernible as such, and the protoplasm having got rid of the unstainable granules, condenses and thus appears more deeply stained. As the secretory granules move from the peripheral to the central end of the cell on their way to the lumen, it follows that the peripheral end of the cell is the first to revert to the unloaded state, and in this stage of secretion two zones in the cells of the alveoli may sometimes be made out—a peripheral next to the basement membrane, in which the protoplasm is condensed and stains deeply; and a central, surrounding the lumen, still containing secretory granules, and hence more lightly stained. But these zones are never to be so distinctly seen as in the cells of the alveoli of the pancreas, and indeed in prepared specimens of the parotid are practically never seen. When completely exhausted the cells are small, shrunken, granular and deeply stained, the nuclei being clearly seen, and sometimes a distinct lumen; but for this state of complete exhaustion to ensue prolonged faradisation of the nerve to the gland is necessary.

The alveoli of the **sublingual**, a wholly mucous gland, are larger than those of the parotid, and their outline is a little different, being more circular, or made up of the segments of more than one circle. They are surrounded by a distinct basement membrane, the flattened nuclei of the cells forming it being often very conspicuous. In the resting state of the gland the cells are large, and in prepared specimens translucent and faintly stained, the nucleus being displaced to the base, sometimes into one corner.

The translucency* is due to the accumulation in the cells of granules of *mucinogen*, the precursor of mucin, the protoplasm remaining as a delicate network, usually invisible, in the meshes of which the granules lie. Sometimes a little protoplasm, free from mucinogen, may be seen condensed round the nucleus of the cell.

When these cells secrete mucin the granules of mucinogen disappear from the protoplasm, the strands of which fall together again as the whole cell diminishes in size. It consequently appears to stain more deeply and to be more granular, and the nucleus returns to the outer third of the cell instead of being

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* In a fresh teased portion of the gland the mucinogen appears as distinct granules. Under the influence of water or dilute acid or alkali the granules swell up into a transparent mass, which is perhaps of the nature of mucin itself. The effect of hardening reagents on the gland cells seems to be similar, so that we require to distinguish between the appearance of the cells in the fresh tissue and in tissue that has been subjected to treatment.

pressed against its basal border. The lumen of the alveolus, often only potential in the loaded gland, becomes now obvious and may be quite considerable. In the process of secretion, as the granules of mucinogen move towards the lumen, the outer part of the epithelium naturally is the first to become free from granules, and the inner part the last to contain them, but it is not usually possible to make out two distinct zones as in the pancreatic cells.

In addition to the mucin-forming cells just described others differing markedly in appearance are to be seen placed here and there between them and the basement membrane. They are granular, stain deeply, and possess a rounded nucleus, and frequently occupy a somewhat triangular space between the bases of two adjacent mucous cells and the basement membrane. They are frequently crescentic in shape and have been termed the "demilunes" or "crescents of Gianuzzi" (Fig. 234). These cells, which are destined to replace the mucous cells proper when these are thrown out in the natural process of decay, vary in the degree in which they are in evidence in different animals and in different situations in the same animal. Thus they are absent from the alveoli of the sublingual gland of the guinea-pig and the submaxillary gland of the mole. In the submaxillary gland of the dog the demilunes occur at intervals; in that of the cat they frequently form a complete investment for the alveoli. The mucous glands of the trachea and œsophagus of an animal may show no demilunes, while they are very distinct elsewhere, as in the epiglottis (sheep), in which they form the greater part of the alveoli.

The **submaxillary** gland of man is a *muco-serous* one, *i.e.*, most of the alveoli are mucous but some are serous, and we have here, therefore, a favourable field for comparison of the two kinds of cells. The mucous alveoli yield mucin, and the serous alveoli ptyalin, so that the saliva of the submaxillary gland contains the essential elements of both the parotid and sublingual secretions; and for the same reason it is not so watery as the one nor so viscid as the other.

Though in man these three glands have the characters indicated above, the corresponding organs in other mammals are not necessarily quite the same in structure. Thus the submaxillary of the rabbit is a serous, that of the dog a mucous gland. Furthermore, the amylolytic activity of the saliva varies much in different animals. In man, the pig and the rat, parotid, submaxillary and mixed saliva all act upon starch, and the submaxillary secretion is often more active than the parotid. In the rabbit the parotid is the most active. As we pass from the rabbit to the cat and dog

we descend in the scale of amylolytic energy of the mixed saliva; in ruminants, such as the horse, ox, and sheep, it has very little power.

The salivary corpuscles found in saliva seem to be either dead leucocytes from the tonsil or cells cast out from the mucous alveoli, for they are absent from the watery secretion of the parotid. They are sharply defined spherical cells about the size of a white blood-corpuscle or a little larger, and consist of an envelop enclosing fine granules, which usually exhibit very distinct Brownian movement. One or more excentrically placed nuclei can generally be seen.

In addition to the three large glands described, there are smaller groups of mucous and serous alveoli scattered beneath the epithelium of the mouth and tongue which open upon the buccal cavity and contribute their quota to the mixed saliva; and these are named from their position lingual, buccal, labial or palatine. An example of small serous glands is afforded by von Ebner's, which open into the fossæ of the circumvallate papillæ at the back of the tongue; while the glands at the base of the tongue, and in the other situations indicated, are of the mucous type.

The **innervation of the salivary glands.**—Like the respiratory and vascular systems, glandular organs are subject to the control of the nervous system, and the salivary glands are no exception to the rule. If some sapid or stimulating substance be placed on the tongue secretion follows as the result of a reflex act through a centre in the medulla, the afferent nerve being in this case the lingual. Stimulation of the glosso-pharyngeal nerve also produces the same result, indeed more vigorously. The terminations of the vagus nerve in the mucous membrane of the stomach may receive the afferent impression, as in the case of gastric irritation previous to vomiting. The centre may also be affected from the higher parts of the

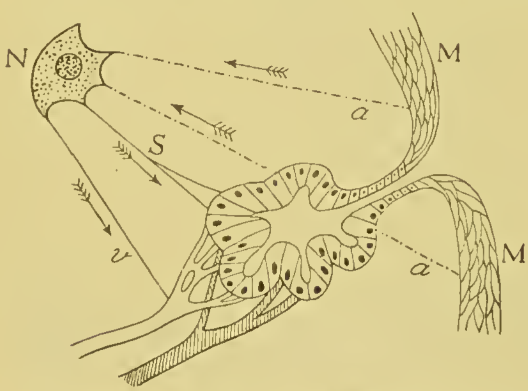

Fig. 236.—Diagram of Innervation of a Salivary Gland.

N, Nerve centre; *M*, mucous membrane of mouth; *a*, afferent nerves from mucous membrane to nerve centre; *S*, secretory nerve from nerve centre to gland cells; *v*, vasodilator nerve from nerve centre to blood-vessels.

brain, either in the way of inhibition or stimulation, as when the mouth becomes parched from fear or when the sight or thought of food produces a flow of saliva. From the foregoing it will be gathered that though the mouth is always kept moist, the flow of the saliva in any considerable quantity is intermittent and is usually excited by the taking of food. The amount secreted daily is considerable, being estimated at 1 to 2 litres. We may consider the nervous paths concerned in the act of secretion first in the submaxillary and sublingual glands, in which it has been specially studied.

The submaxillary gland receives two sets of efferent nerve-fibres—(1) a branch of the chorda tympani, and (2) fibres from the cervical sympathetic.

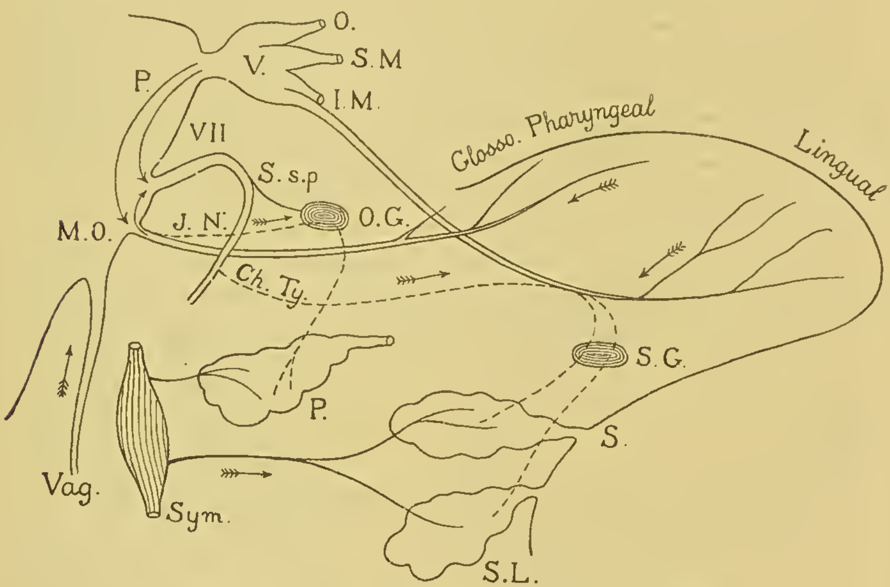

Fig. 237.—INNERVATION OF SALIVARY GLANDS.

P., Pons; *M.O.*, medulla oblongata; *J.N.*, Jacobson's nerve; *O.*, *S.M*, and *I.M.*, ophthalmic, superior maxillary, and inferior maxillary divisions of fifth nerve; *VII.*, seventh cranial nerve; *S.sp.*, small superficial petrosal; *Vag.*, vagus; *Sym.*, sympathetic; *O.G.*, otic ganglion; *S.G.*, submaxillary ganglion; *P.*, *S.*, and *S.L.*, parotid, submaxillary and sublingual glands; *Ch. Ty.*, chorda tympani nerve.

The *chorda tympani* leaves the facial nerve in the Fallopian canal and passing through the tympanic cavity (hence "chorda tympani") joins the lingual nerve, and many of its fibres pass with it to the tongue. Others branch off as a delicate filament which runs along the duct of the submaxillary gland to the gland itself, giving off a branch to the sublingual. As the fibres enter the hilus of the submaxillary they join the nerve-cells, which are

abundant there, and which form a special group (Langley's ganglion), losing at this point their medullary sheaths. Nerve-cells are also found appearing in the course of the nerve as it runs along the duct (Wharton's).

On reference to Fig. 237 it will be seen that the lingual nerve, Wharton's duct, and the chorda tympani form a triangle—known as the chorda-lingual triangle. In this are found numerous ganglion cells and, in addition, a special collection known as the "submaxillary ganglion." This is, however, an incorrect appellation physiologically, as the cells are placed on fibres passing to the sublingual. This has been proved by Langley's nicotine method. The application of nicotine to the chorda-lingual triangle does not block impulses passing down the fibres on the cranial side of the cells from reaching the submaxillary gland, while it does do so in the case of the sublingual. (It will be recollected that nicotine first paralyses ganglion cells without affecting the nerve-fibres.) This method has also established the fact that the vaso-dilator fibres of the chorda are connected with ganglion cells in the same situations as the secretory fibres.

These ganglion cells are local cell stations merely and not seats of peripheral reflex action, Langley's ganglion being the cell station for the submaxillary gland, and the so-called "submaxillary" ganglion that for the sublingual.

The *sympathetic* fibres (Fig. 237) are derived from the superior cervical ganglion and are for the most part non-medullated. In the cord and between the cord and the ganglion they follow apparently the same path as the vaso-constrictor fibres. They pass to the gland along its small arteries.

Now, if the cervical sympathetic be divided and the afferent lingual nerve stimulated secretion of saliva takes place as before, but if the chorda be divided instead no reflex secretion will take place; so that so far as ordinary secretion is concerned the gland is supplied by one set of efferent fibres alone—those of the chorda tympani—through which reflex secretory effects may be brought about. The question now arises—How is the secretion induced by these impulses transmitted by the chorda?

If the chorda be divided and the peripheral end stimulated, a copious comparatively-watery secretion takes place and the blood-vessels of the gland are found dilated. We have previously referred to this dilatation of the arterioles of the gland whereby the resistance at the arterio-capillary junction disappears, the capillaries become dilated, and the veins which contain arterial blood exhibit a distinct pulse. The question naturally arises—Is the secretion the result of the vascular dilation? and this we must

answer in the negative. That dilatation itself cannot produce secretion is shown by the action of atropin: if this drug be injected, stimulation of the peripheral end of the chorda produces dilatation but no secretion. Again, if Wharton's duct be obstructed the pressure of the saliva in it may rise considerably above that of the blood-pressure in the arteries. Thirdly, if an animal be decapitated and the chorda stimulated secretion takes place—clearly here independently of any vascular pressure. From these experiments it is concluded that the chorda contains two sets of fibres—*secretory* and *vaso-dilator*; and though secretion is not dependent on the temporary dilatation of the vessels for its occurrence, nor can dilatation *per se* result in secretion, it is undoubted that the two run side by side and have an important relation to each other; the stimulated gland requiring a liberal supply of blood and the substances the blood brings with it to maintain its activity and a rapid removal of the waste products of its activity, which the increased blood-stream carries away.

The secretion therefore seems to be the result of impulses conveyed to the gland, *i.e.*, to its cells, by special secretory fibres contained in the chorda tympani, but anatomical continuity between these fibres and the gland cells has not yet been satisfactorily demonstrated except in the case of the salivary gland of the cockroach.

The cervical sympathetic contains *secretory* and *constrictor* fibres, and if it be stimulated the vascular result is the opposite, viz., that of constriction of the vessels. The amount of saliva secreted too is trifling, particularly viscid, and rich in salivary corpuscles and amorphous lumps of mucin, so that the degree of vascular dilatation seems to decide whether the secretion is watery (as on stimulation of the chorda) or viscid (as on stimulation of the sympathetic). We thus speak of "chorda" and "sympathetic" saliva.

Like the submaxillary and sublingual gland, the parotid is supplied with two sets of efferent fibres—(1) The cerebral, which pass from the tympanic branch of the glossopharyngeal nerve with the small superficial petrosal to the otic ganglion, and then by the auriculo-temporal of the fifth to the gland. Stimulation of these cerebral branches in the dog gives rise to a copious watery secretion, while that of (2) the sympathetic fibres (derived, as in the case of the submaxillary and sublingual glands, from the superior cervical ganglion) yields little or none. When the two are stimulated at the same time the saliva secreted is much richer in organic matter than when the cerebral fibres are stimulated alone; and though stimulation of the sympathetic by itself

produces no secretion it must not be inferred that it is without result. On the contrary very marked changes are to be observed in the gland cells, which become smaller, the nuclei round and large, and their protoplasm more deeply stainable. In fact, in the dog and rabbit the changes in the gland cells following stimulation of the sympathetic fibres are more marked than those following stimulation of the cerebral. The stimulation of the latter seems, in short, to promote the flow of water through the cells into the lumen of the gland, while sympathetic stimulation increases the discharge of organic material.

After prolonged excitation of either the sympathetic or cerebral fibres to these glands, increase of stimulation produces no increase in the percentage of organic matter present in the saliva, while the inorganic salts and water are still increased, and this result agrees well with what we should expect to find. The production of the organic part of the secretion requires time, and is the outcome of processes going on in the gland cells during a period of rest, as the result of which they become laden with granules of the precursors of secretion; whereas the water and salts require no such elaborate preparation and are merely seized upon *en passant* in the blood. We have used the expression "seized upon" advisedly, for they are not received into the cells by a mere process of filtration, but withdrawn by them from the blood, *i.e.*, from the lymph, by their own vital activity, and passed unchanged into the lumen of the gland tube.

The precise explanation of the difference in cerebral and sympathetic secretion is at present not forthcoming. According to Heidenhain there are two sets of secretory fibres—(1) Those which are *secretory* proper and cause a flow of water into the lumen of the alveolus; (2) those which are *trophic* and concerned (*a*) with the solution of the already-formed secretion granules, and (*b*) with the growth of the protoplasm of the cell itself. According to his theory the chorda in the case of the submaxillary gland contains a preponderance of secretory fibres and a minority of the trophic ones, and hence the wateriness of its secretion; while the sympathetic has a majority of trophic fibres, and hence the thickness and scantiness of the secretion resulting from stimulation of it. Such a theory is convenient and it may be near the truth, but there is not any very distinct evidence in proof of it. At present we really know too little of the inner complicated workings of any gland cell, and how these workings are regulated by nervous influence, to justify us in accepting such a simple explanation, in the way of which, too, there are several difficulties which need not, however, further detain us here.

The position of the **salivary centre** is in the medulla, apparently in the region of the vaso-motor centre. If the brain be removed down to the medulla stimulation of afferent nerves will still induce salivation; but if the medulla be destroyed no result is obtained. Further, stimulation of the medulla itself will cause secretion.

Paralytic secretion.—If the chorda be divided on one side a thin watery secretion is discharged at the end of twenty-four hours by the submaxillary gland of the same side, and this is known as "paralytic secretion." A similar but less copious flow occurs from the same gland on the opposite side, and to this the name of "antilytic" secretion has been given. The paralytic secretion increases up to the eighth day, after which it gradually diminishes, while the gland degenerates.

During the later stages of the secretion it appears to be due to excitement in the local nervous mechanism of the gland itself, as division of the sympathetic has no effect upon it. During the first few days, however, the secretion seems to have its origin in the medullary centre, as division of the sympathetic on the same side will lessen or arrest it.

Mastication.

Mastication is one of the muscular phenomena of digestion, and consists in the trituration of the food by the grinding movements of the teeth upon each other, resulting from the up and down, forwards and backwards, and lateral movements of the lower upon the upper jaw. Mastication is also aided by the movements of the tongue and the muscles of the cheeks and lips.

The *temporal*, *masseter*, and the *internal pterygoid* muscles raise the jaw, while the *digastrics*, the *genio-hyoids* and the *mylo-hyoids* depress it. It is pulled forwards by the *external pterygoids*, and backwards by the lower horizontal fibres of the temporals. The pterygoids of one side acting alone direct the jaw to the other. The *buccinator* muscle and the *orbicularis oris* confine the food to the cavity of the mouth proper, and prevent it finding a lodgment outside the line of the teeth, between them and the lips and cheek. The tongue mixes the food as it is divided and crushed by the teeth with saliva, and rolls it into a bolus, in preparation for the process of deglutition.

With regard to the structure of the parts concerned, that of the teeth has been already referred to and need not again be mentioned here. The three molars on each side above and below

are the teeth more especially concerned in grinding the food, while the incisors in front are used for cutting purposes, the bicuspids at the sides occupying an intermediate position. The mouth generally is lined by stratified squamous epithelium resting upon a submucous layer of connective tissue (containing blood-vessels, lymphatics and nerves, and here and there small mucous glands) which intervenes between it and the subjacent parts, which necessarily vary in different situations. Thus where the epithelium covers the jaw we find bone beneath the submucous layer, and where it lines the inner side of the cheek or the tongue, muscle.

The tongue itself consists of a series of both intrinsic and extrinsic muscles bound together by connective tissue, the whole being invested with the same tissue and covered with epithelium

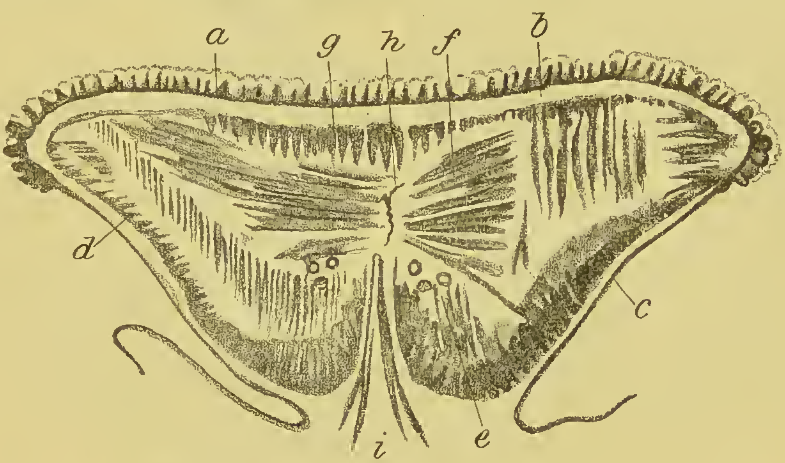

Fig. 238.—Vertical transverse section of Tongue of Dog.

a, Epithelium of dorsum of tongue raised into papillæ; *b*, subepithelial connective tissue; *c*, epithelium of inferior surface; *d*, inferior longitudinal muscle; *e*, transverse section, lingual artery and nerve; *f*, radiating muscle; *g*, superior longitudinal muscle; *h*, median raphé; *i*, extrinsic muscle.

of the same kind as that lining the mouth generally, except that it is raised into papillæ in parts and otherwise modified to subserve the function of taste; but these points we shall take up when the "senses" are under consideration. The intrinsic muscles form the great mass of the tongue itself and control its smaller movements, *i.e.*, those concerned with the changes in shape of the organ itself. The extrinsic muscles, on the other hand, attach the tongue and neighbouring parts, and regulate its movements in relation to these parts, thus controlling the more general movements of the organ as a whole. The accompanying diagram shows some of the intrinsic fibres

of the tongue as they appear when that organ is cut transversely. The *superior* and *inferior longitudinal* fibres are here seen cut across; the *transverse* fibres passing out from the median raphé (*f*) and the *vertical* fibres between the upper and lower surfaces of the tongue are seen cut longitudinally. The action of each of these sets of fibres in altering the form of the tongue depends largely on whether they act singly or together, and if the latter, in what combination. Thus, if the dorsal muscular fibres contract by themselves they will raise the tip of the tongue; but if they act at the same time as the ventral fibres, the two sets together will shorten the tongue and thicken it. And so with all the fibres, there being virtually no limit to the possible combinations, so that such a co-ordination is possible as will enable the tongue to assume any form requisite to meet the necessities of its function; and in this connection it will be remembered that it is an organ of speech as well as digestion.

At *i* in Fig. 238 is seen the termination of one of the extrinsic muscles, which include the *hyoglossus*, *palatoglossus*, *geniohyo-glossus*, *styloglossus*, &c., the names of which indicate their attachments to some extent. For an exact account of their relationships the student is referred to works on Anatomy.

The nerves to the tongue are the hypoglossal, supplying the muscles; the lingual of the fifth and the glossopharyngeal are the afferent branches. The fifth is the motor nerve to the muscles of the jaws, and the sensory nerve for the mouth generally; the buccinator and orbicularis oris are supplied by the facial nerve.

Deglutition.

When the food has been masticated in the mouth, and is collected as a bolus on the dorsum of the tongue, a considerable effort is yet required to enable it to reach its first stopping place—the stomach; and the muscular process by which it is enabled to travel the intervening distance is called the act of *deglutition*, or, in common parlance, "swallowing." This act may be divided into three stages, of which the first is voluntary and the two last involuntary; but no very hard and fast line can be drawn where volition ends and the purely reflex character of the movement commences. As a whole, deglutition is a reflex act, started voluntarily by the movements of the jaws and tongue bringing food into contact with the fauces—the afferent receiving surface of the reflex arc. In the first (voluntary) stage the bolus of food is pressed back by the dorsum

of the tongue through the anterior pillars of the fauces—the "isthmus faucium"—and after it has reached this spot the act is certainly purely reflex. The second part of the course of the food lies through that portion of the pharynx common to both respiration and deglutition; while the third is through the lower part of the pharynx, formed by the middle and lower constrictors and the œsophagus. Before dealing with these three stages it may be well to say a few words as to the structure of the parts named.

The **pharynx** lies between the mouth and œsophagus, and is composed largely of the three constrictors—superior, middle, and inferior. These muscles are lined internally and externally

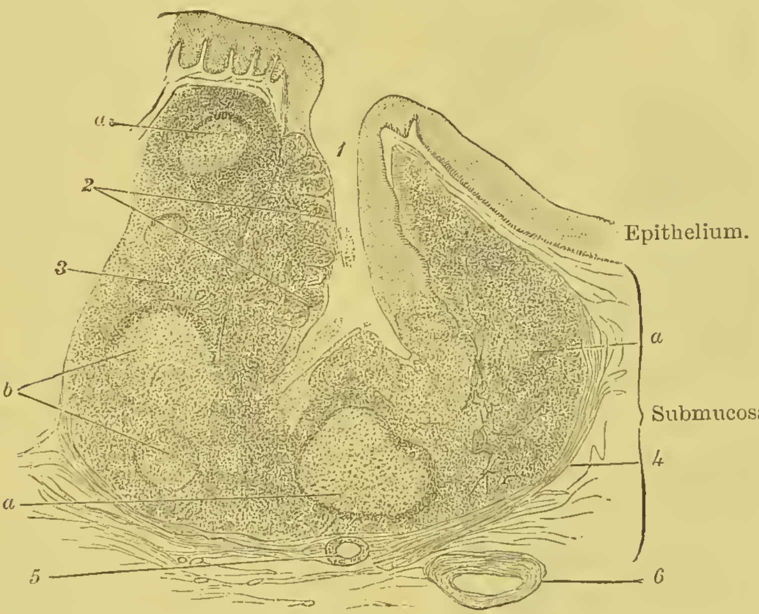

Fig. 239.—SECTION THROUGH CRYPT OF TONSIL (× 20).

1, Entrance to crypt; 2, epithelium infiltrated with leucocytes; 3, adenoid tissue; 4, fibrous sheath or sac; 5, transverse section of duct of mucous gland; 6, transverse section of blood-vessel; *a* and *b*, lymphoid nodules.

with fascia, the internal fascia being especially marked, and known as the "pharyngeal aponeurosis." On the inner side of the pharyngeal fascia is a submucous layer of connective tissue, and within that a layer of epithelium, both being continuous with the similar layers in the mouth. In the upper part of the pharynx, into which the nares open, the epithelium, though continuous with that of the mouth, unlike it, is ciliated; in the part of the pharynx concerned in swallowing, however, the epithelium is of the stratified squamous variety and similar

to the buccal epithelium generally. Beneath the epithelium of the pharynx are found scattered mucous gland follicles.

The *anterior pillars of the fauces* are folds of the epithelial and connective tissue layers containing the *palato-glossi* muscles; while the *posterior pillars* contain the *palato-pharyngei*. Between the two pillars on each side is to be observed a small eminence —the *tonsil*.

The **tonsil** is a collection of lymphoid follicles which surround small crypts of epithelium—involutions of the general epithelial lining, some 15 in number, into the submucous tissue beneath. The lymph nodules are imbedded in less dense adenoid tissue, which lies immediately below the epithelium, and the whole mass is to some extent defined from the surrounding parts by a condensation of tissue at the periphery forming a kind of sac. The epithelium is often eroded from below by the lymphoid tissue, and in this way leucocytes from it are able to make their way into the cavity of the mouth, and are found in the saliva as salivary corpuscles. The illustration shows this erosion of the epithelium lining one of the crypts (Fig. 239).

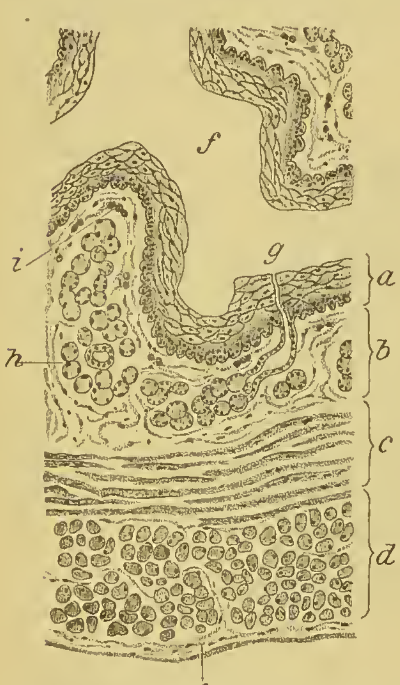

Fig. 240.—Transverse Section of Œsophagus of Pig.

a, Epithelium; *b*, subepithelial connective tissue; *c*, internal circular muscular coat; *d*, external longitudinal muscular coat; *e*, fibrous tissue investment; *f*, lumen of œsophagus; *g*, opening of duct of mucous gland; *h*, group of mucous alveoli, with duct in centre cut transversely; *i*, isolated strands of muscularis mucosæ.

The **œsophagus** is the continuation of the pharynx below, and ends in the cardiac end of the stomach. It has three coats —mucous, submucous and muscular; the latter being invested externally with a fibrous covering and composed of two layers of muscle fibres—internal circular and external longitudinal. In the upper part of the tube where the muscular layer is continuous with the constrictors the fibres are of the striped variety, but these become replaced as we pass down by non-striped fibres, and as the stomach is neared only the latter kind are found. The submucous coat lies within the

muscular coat, and in the lower half or third of the œsophagus: the alveoli of many mucous glands are found in it, their ducts piercing the mucosa to reach the lumen of the tube. Within the submucosa is the mucous coat itself, the junction of the two being marked by the presence of bands of longitudinally running non-striped muscle fibres—the *muscularis mucosæ*—which do not, however, form a continuous sheath. The epithelium lining the mucosa rests on a connective tissue basis, and is of the stratified squamous variety; here and there may be seen the ducts of the mucous glands below opening on its surface. In the undistended state of the œsophagus its walls fall together, so that the lumen in ordinary section is seen as a more or less irregular stellate fissure, and not as a circular aperture. This characteristic is to some extent indicated in Fig. 240, though only a portion of the lumen is visible.

We may now return to the consideration of the passage of the bolus of food through these portions of the alimentary canal. When it has passed the anterior pillars of the fauces, or a little previous to this, the soft palate is raised by the *levator palati* towards the posterior wall of the pharynx, and the latter is projected forwards to meet it by contraction of the superior constrictor. In this way the pharynx becomes shut off from the posterior nares, so that the food cannot pass into the upper respiratory region, the shutting off being made more complete by contraction of the *palato-pharyngei* muscles in the posterior palatine arches, whereby they are brought close together, the gap between them being closed by the uvula. At the same time the food is prevented from passing back into the mouth by contraction of the *palato-glossi* muscles in the anterior pillars of the fauces, which approach each other and thus leave a smaller space to be covered by the back of the tongue. It only remains now to ascertain how the food is prevented from going down the wind-pipe. As the food passes the back of the tongue, the arytenoid cartilages are drawn together, approximating the vocal cords, the epiglottis is turned backwards like a leaf covering the opening, and the thyroid cartilage with the larynx is lifted up so that it lies under the overhanging root of the tongue and so abets the action of the epiglottis.

Thus the entrance to the larynx being closed, and the passage of the food in the one direction being in every way facilitated, it follows that course and is received by the middle and inferior constrictors of the pharynx, which is raised as a whole to meet it by the *stylo-pharyngei* and *palato-pharyngei* muscles. The constrictors contract from above downwards and force the food

into the œsophagus, along which it is driven by a succession of similar contractions on into the stomach. When the food is liquid, however, the contractions of the œsophagus may often be dispensed with, and even of the constrictors of the pharynx, the fluid being shot along the tube as along a shaft by the impulse it received in the mouth from the tongue and the muscles of the floor of the mouth; but in such a case a contraction of the œsophagus succeeds the act of swallowing, or rather the passage of the fluid, as if to ensure the completion of the act.

As will be seen from the above description the most important part of the passage of the food between the mouth and the stomach is when it is crossing the respiratory part of the pharynx, when there is a danger of its taking either of two false directions —(1) into the nose, or (2) into the larynx; of going, in fact, the "wrong way." It is in this part of its course that its rate of progression is the quickest, being slower in the first stage in the mouth, and again in the third stage in the lower part of the pharynx and the œsophagus, when the dangerous area has been passed.

The centre for deglutition lies in the medulla oblongata, perhaps in the superior olivary bodies. The afferent impulses for the reflex act reach it by the glosso-pharyngeal nerve for the tongue and fauces, by the palatine branches of the fifth for the soft palate, and by the superior laryngeal branches of the vagus to the glottis and epiglottis. The motor nerves to the muscles include the hypoglossal to the tongue; the branches of the fifth to the digastric, mylo-hyoid and muscles of mastication; the glosso-pharyngeal to the muscles of the pharynx; the inferior laryngeal to the muscles of the larnyx; and the facial branch to the levator palati.

Œsophageal peristalsis.—The wave of contraction passing along the œsophagus is one of "peristalsis," as it is termed, and in many ways resembles the corresponding movement of the intestinal walls. It is mainly due to a local descending contraction of the circular fibres of the muscular coat, aided and accompanied by contraction of the longitudinal coat, which pulls the tube up over the bolus as it descends. This power of peristaltic action is to some extent inherent in the œsophagus itself, but for the most part it is under the control of the nervous system, and indeed strikingly so. Thus, if a portion of the tube be excised or ligatured, so that its continuity is interrupted, and a wave of peristalsis started by stimulating the lining of the pharynx, it will pass across the cut or other interruption and pursue its course through the whole length of the tube through

the connections of the latter with the central nervous system. The afferent nerves for the production of this movement are the superior laryngeal and pharyngeal branches of the vagus, branches of the fifth and of the glosso-pharyngeal; the efferent impulses passing down the vagus through the recurrent laryngeal to the upper part of the œsophagus and through the œsophageal plexus to the lower part.

When the bolus of food arrives at the lower end of the œsophagus the circular muscular fibres at the cardiac end of the stomach, which form a kind of sphincter in this region, and ordinarily by their tonic contraction prevent the regurgitation of food, relax, and the food is received into the cavity of the stomach itself, the sphincter closing again behind it.

Gastric Digestion.

Structure of the stomach.—The wall of the stomach is made up of three coats, continuous with those of the œsophagus, the whole being surrounded with a peritoneal investment. The mucosa, unlike that of the œsophagus, is lined by a layer of columnar epithelium, which is involuted to form numerous simple or divided gland tubes, arranged side by side vertically to the surface of the other layers. The food in the stomach is thus brought into intimate relation with the secretion of the organ at its origin, as contrasted with the state of affairs in the mouth, which the saliva only reaches after traversing a long duct.

The glands of the mucosa are of two kinds—the *cardiac* and *pyloric*: the former, as the name implies, being found in the cardiac region of the stomach, while the latter occur at the pyloric end. The **cardiac glands** are sometimes simple tubes, but more often the lower two-thirds or three-fourths of the tube is divided into two or three. The part below the point of division is termed the *fundus*, the point of division itself marks the *neck*, while the portion above the neck is the *mouth* of the gland. The mouth or duct (*a*, Fig. 241) is short compared with the fundus; its lumen is wide and lined by columnar cells continuous with the immediate lining of the stomach itself from the mouth of one gland to that of its neighbour. These columnar cells are mucin-forming, the inner two-thirds being clear and homogeneous and staining lightly, while the outer or basal third contains the nucleus, surrounded by a little granular protoplasm which stains more deeply. Seen in surface view these cells present the appearance of an hexagonal mosaic, their outlines being clearly defined. They are tallest on the ridges between the glands and become shorter as

the neck is reached. The neck marks the junction of the fundus, or secreting part proper of the gland, and the mouth or duct, and here the character of the cells changes.

The fundus is lined by two kinds of cells—the *chief*, or *central*, and the *parietal*. The chief cells are columnar in shape and form

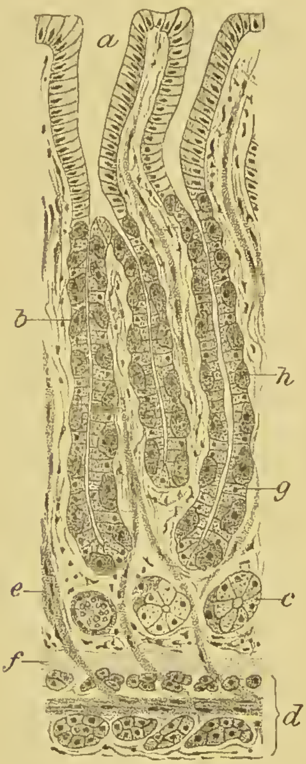

Fig. 241.—VERTICAL SECTION OF MUCOUS MEMBRANE OF CARDIAC END OF STOMACH OF CAT.

a, Duct of gland; *b*, gland tubule; *c*, gland tubule cut transversely; *d*, muscularis mucosæ sending *e*, muscular strands, between the gland tubules; *f*. clear homogeneous layer; *g*, central or chief cells; *h*, parietal cell.

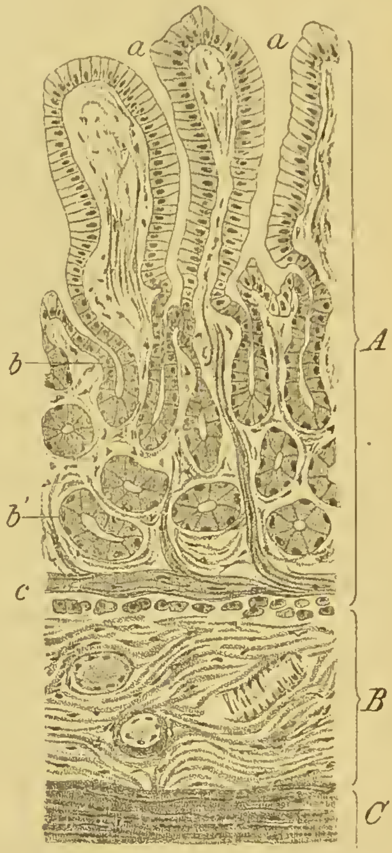

Fig. 242.—VERTICAL SECTION OF PYLORIC END OF STOMACH OF CAT.

A, Mucosa; *B*, submucosa; *C*, muscular coat; *a*, ducts of glands; *b*, gland tubules; *b′*, gland tubule cut across; *c*, muscularis mucosæ.

a continuous lining to the secreting part of the tubule. They are faintly granular in appearance, with indistinct outlines, and possess a rounded nucleus placed towards their base. The lumen they surround is narrow and tortuous as contrasted with that of the mouth of the gland. The parietal cells differ from the central

in being scattered, that is to say, they do not form a continuous layer and are placed outside the others, between them and the basement membrane, and thus do not reach the lumen of the tube, from which they are separated by the chief cells; an exception to this, however, occurs in the region of the neck, where they are more numerous and frequently project inwards between the chief cells so as to abut upon the lumen. The parietal cells are nucleated, large compared with the chief cells, ovoid in shape, with a distinct outline, coarsely granular, and stain deeply with reagents such as aniline dyes.

The **pyloric glands**, on the other hand, though resembling in a general way those found at the cardiac end of the stomach, differ in some important particulars, of which the most marked is the absence of the parietal cells. Their ducts are longer and wider and their bodies proportionately shorter than is the case with the cardiac glands, so that the duct is usually at least as long as the secreting part itself, and indeed sometimes twice as long. The lumen of the tubules, too, is wider than is the case with the cardiac glands, and as already stated is surrounded only with chief cells.

The epithelium, though the most important, is only one part, however, of the mucosa. Surrounding the gland tubes and filling the space between them and the muscularis mucosæ is a basis of delicate adenoid tissue with lymph-corpuscles in its meshes, the surface of the tissue beneath the epithelium being condensed to form a basement membrane. Supported by the adenoid tissue is a capillary network surrounding the gland tubes—a network supplied with blood by branches from larger vessels in the submucosa. Strands of non-striped muscle also run up between the gland tubes from the *muscularis mucosæ* (*d* and *c*, Figs. 241 and 242), which forms the external limit of the mucous membrane. It consists of two layers of non-striped muscle—an inner circular and an outer longitudinal. As in the œsophagus the mucosa as a whole is thrown into folds, or rugæ, when the stomach is empty and contracted, which only become flattened out when it is full and distended; this folding of the mucosa being possible here as elsewhere through the looseness and elasticity of the submucous coat beneath it, which permits of free movement of the inner coat on the muscular wall outside.

The submucosa consists of loose connective tissue of the areolar type and contains blood-vessels, lymphatics, and a plexus of nerves corresponding to Meissner's in the intestine. The large arteries give off branches which pierce the muscularis mucosæ and run vertically between the gland tubes, giving off subdivisions to the capillary plexus as they go; and from the capillary plexus

venous trunks in turn arise which pass through the muscularis mucosæ themselves to join the larger veins in the submucosa. A somewhat similar arrangement holds with the lymphatics.

Outside the submucous is the muscular coat of the stomach, consisting of two layers—an internal circular and an external longitudinal; but the inner part of the circular layer runs somewhat obliquely, and is sometimes described as a third division. Between the longitudinal and circular layers is a plexus of nerve-fibres, continuous with Auerbach's plexus in the intestine.

At either orifice of the stomach the circular fibres are developed to form a sphincter, which is particularly marked at the pylorus. The œsophagus opens into the larger cardiac portion of the stomach, while the duodenum is continuous with the smaller pyloric portion; the junction between the two being marked by a thickening of the circular fibres. The portion of the stomach on the pyloric side of this thickening is sometimes termed the *antrum of the pylorus*, and the thickening itself the *sphincter of the antrum*. As we shall see in considering the movements of the stomach during digestion, after food is taken contractions commence at the level of this band of circular fibres and run towards the pyloric sphincter proper. Outside the muscular coat is the peritoneal, a thin sheet of connective tissue covered with polygonal squamous cells.

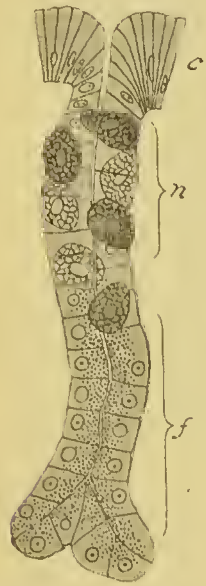

Fig. 243. — Gastric Gland of Mammal (Bat) during activity. (Langley.)

c, Mouth of gland, with its cylindrical cells; *n*, neck, containing conspicuous ovoid cells, with their coarse protoplasmic network; *f*, body of the gland.

Changes in the gland cells during secretion.—The gastric cells (chief) exhibit analogous differences to those of the salivary glands in their loaded and discharged states, though these changes cannot so readily be examined in the living gastric membrane. Previous to secretion the chief cells are studded with minute granules distributed evenly throughout the cell substance, while during digestion the granules leave the outer part of the cell and are found only next to the lumen. In the prepared stained specimen differences between the loaded and exhausted cell are also observable, though, as in the case of the salivary glands, the action of the reagent used may mask the natural appearances. Before digestion the cells are finely granular, pale,

and lightly stained; as digestion commences they become swollen, more granular, and stain more deeply. Later they are shrunken, still more granular and more deeply stained. Here, as before, the cell loaded before secretion commences does not stain deeply on account of the quantity of dead material—the precursor of the secretion—accumulated in the meshes of the protoplasm, or material at all events which has ceased to have the stainable character of living protoplasm.

The ovoid parietal cells swell up when digestion commences, but do not exhibit any characteristic granules. After secretion they are smaller and more coarsely granular than before.

The chief cells of the cardiac glands and the cells of the pyloric glands secrete the pepsin of the gastric juice, while the parietal ovoid cells of the cardiac glands secrete the hydrochloric acid. In Heidenhain's experiment on the stomach of dogs, the fundus of the stomach of one and the pyloric part of the stomach of another were converted into cul-de-sacs. In the first a secretion containing acid and pepsin was found, and in the other an alkaline secretion containing pepsin.

Innervation of the stomach.—The nerves of the stomach are derived from the right and left vagi and the sympathetic. The fibres of the latter leave the spinal cord by the anterior roots of the spinal nerves from the fifth to the eighth thoracic and pass to the solar plexus and thence to the stomach. The vagi and sympathetic nerves are related both to the secretion of the glands and the movements of the muscular walls, but our knowledge of the extent of their influence under normal conditions is not very definite. The peristaltic movements of the stomach are more independent of the central nervous system than those of the œsophagus, for such movements readily follow on direct stimulation when the organ is entirely separated from its nervous connections, and are probably then due to the influence of Auerbach's plexus between the muscular coats. On the other hand indirect stimulation through the vagus nerve will cause strong peristaltic movements. The question thus arises as to whether normally the movements of the stomach are due to direct stimulation of its muscular wall by the presence of food or to a reflex stimulation transmitted through a centre in the medulla, in which case the vagi would contain both the efferent and afferent fibres involved. That the stomach is not dependent on such a reflex mechanism for its movements is proved by the fact that the introduction of food will still result in peristalsis, even after the vagi have been divided. At the same time there can be

little doubt that normally the movements are the result of such a reflex stimulation as well as the direct one, for if a loop of an animal's intestine be isolated from all its connections except those with the central nervous system, peristalsis may be induced in it by the act of swallowing or even the smell of food. The splanchnic nerves contain inhibitory fibres and when they are cut and the peripheral ends stimulated the movements of the stomach and intestines cease, so that they are thus antagonistic to the vagi. They are further antagonistic in that stimulation of their peripheral ends causes contraction of the blood-vessels, while the vagi contain vaso-dilator fibres.

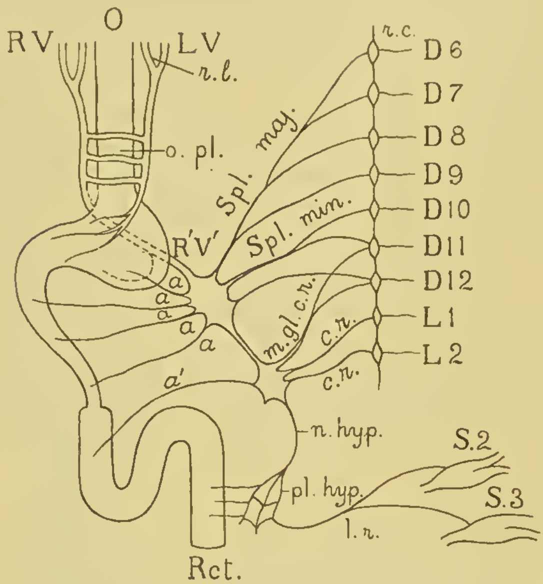

Fig. 244.—Diagram of Nerves of Alimentary Canal.

O, Œsophagus; *Rct.*, rectum; *LV*, left vagus passing in front of stomach; *r.l.*, recurrent laryngeal; *R.V.*, right vagus, passing behind stomach and continued as *R′V′* to join solar plexus; *o.pl.*, œsophageal plexus; *a*, branches from solar plexus to stomach and small intestine; *a′*, branches from inferior mesenteric ganglion to large intestine; *Spl. maj.*, great splanchnic nerve; *Spl. min.*, small splanchnic nerve; *mgl.*, inferior mesenteric ganglion; *n.hyp.*, hypogastric nerve; *pl.hyp.*, hypogastric plexus; *r.c.*, rami communicantes; *c.r.*, nerves from the ganglion, &c., belonging to eleventh and twelfth dorsal and first and second lumbar nerves; *l.r.*, nerves from the second and third sacral nerves, *S2*, *S3*.

Secretory nerves of the stomach.—If the mucosa be locally stimulated, as by a feather, a small amount of secretion results, but the presence of food itself calls forth a much greater quantity and the membrane becomes flushed with blood from dilatation of its vessels. To what extent the food acts locally as a stimulant to the glands and to what extent through the central nervous system is still a matter of doubt. That the central nervous system is capable of influencing the gastric glands is clearly shown by Pawlow's experiments on dogs. He made a gastric fistula by incising the abdominal and gastric walls and stitching the margins of the two openings together, and then divided the œsophagus in the neck, connecting the two open ends of the tube with the exterior in the same way. Through

the lower of these two openings the animals were fed and kept alive.

He found that the mere act of masticating and swallowing food, which of course issued from the upper of the two œsophageal openings on the exterior and never reached the stomach, led to a copious secretion of gastric juice, which in this case must have been due to reflex action and independent of any local effect on the stomach itself as the food did not reach it. The vagi would appear to be the efferent nerves concerned, for after section of them below the origin of the recurrent laryngeal no reflex secretion was observed. That the secretory fibres are in the vagus is also to be inferred from the fact that stimulation of the peripheral end of the cut nerve (after sufficient time has been allowed to enable the cardio-inhibitory fibres to degenerate, otherwise the heart is stopped by the stimulation) is followed by secretion. That the splanchnics are not the efferent secretory nerves to the stomach is shown by the fact that in the above experiment reflex secretion still took place after both nerves were cut. At the same time it must be borne in mind that even after the vagi (and splanchnics) have been divided the introduction of food into the stomach still causes secretion of gastric juice, so that some purely local mechanism must in this case be effective, but we do not know the precise nature of it. It seems to be clear that the absorption of the products of digestion has an important influence in stimulating the glands to secretion, as shown by Heidenhain's experiment. He cut out a part of the fundus of the stomach and stitched it to the opening in the abdominal wall in such a way as to make a small independent sac. The edges of the remaining parts of the original organ he sutured together so as to make a complete but smaller stomach. When food was introduced into the main stomach the amount of secretion in the secondary sac was found to vary with the amount of digestion taking place. If the substance introduced was readily digestible a copious flow resulted in the secondary sac; on the other hand, if undigestible material, such as pieces of ligamentum nuchæ, had been introduced very little secretion appeared in the isolated portion of the stomach. This experiment certainly seems to show that absorption of the products of digestion into the blood-stream stimulates the glands, either locally or through the central nervous system, and this is the physiological explanation of the time-honoured custom of taking a small quantity of rapidly-absorbable soup before commencing the more serious work at the dinner table.

We may perhaps, until further evidence is forthcoming as to the precise mechanism involved in gastric secretion, say that the

glands are stimulated partly by—(1) The mechanical effect of the presence of food; (2) a reflex act taking place through the central nervous system; (3) the presence in the blood of the absorbed products of digestion acting (*a*) locally on the glands themselves or (*b*) on the centre in the medulla. At present, however, we cannot assign to these three factors their relative importance.

Gastric juice.—Gastric juice as obtained unmixed with food from a gastric fistula is a clear colourless fluid of a specific gravity of 1002–1005, with a sour taste and smell. Of the solids contained in it part are inorganic and part organic, the former consisting for the most part of alkaline chlorides and the latter being represented by the ferments *pepsin* and *rennin*, with a little mucin derived from the mucin-forming cells already described. This mucin is not therefore to be regarded as an essential constituent of the gastric secretion proper, but inasmuch as the walls of the empty stomach are kept lubricated by it, of necessity it appears in small quantity in an analysis of the juice. The total solids present amount to about ·5 per cent., of which about half are inorganic and half organic. The reaction of the juice is acid, due to the presence of free hydrochloric acid to the extent in man of about ·2 per cent.; but in the dog and other animals the percentage is often higher. The amount of juice secreted in the 24 hours is high, and may be roughly estimated at something like 5 to 10 litres. The secretion is intermittent, not constant, as will have already been inferred.

After the food enters the stomach the amylolytic action of the saliva continues for some 15 minutes, until, in fact, the increasing secretion of the gastric juice by its acidity renders the salivary ferment inactive and by its digestive action destroys it; but the main change in the food in the stomach results from the action of the juice itself and consists in the solution of proteids by the pepsin and hydrochloric acid, whereby they are rendered non-coagulable by heat and diffusible through an animal membrane. Its action on other food stuffs is insignificant if any. Thus, on starch it has no effect whatever, nor has it more on dextrose. Cane-sugar can be inverted apparently by means of a ferment developed in the mucus secreted by the lining cells, and its presence seems to stimulate the secretion of mucus. On fat gastric juice has no real effect, though it dissolves the envelopes of fat cells and the connective tissue between them.

The action of the gastric juice upon proteids, whereby they are dissolved and converted to soluble *peptones*, as they are called, is

illustrated in the laboratory by juice obtained more artificially than from the gastric fistula, which would be a method entailing considerable inconvenience. The mucous membrane of the stomach of a pig is finely minced, ground up in a mortar with sand, and digested in a large quantity of ·2 per cent. hydrochloric acid at a temperature of 35° to 40°C. Nearly the whole of the membrane passes into solution, and the liquid after filtration is opalescent and has strong digestive properties. It, however, has the disadvantage of containing some of the products of digestion as the membrane itself has been dissolved. Another method, by which the presence of products of digestion may be avoided, consists in taking the minced mucous membrane of a pig's stomach as before and extracting it with glycerine. This glycerine extract is powerfully peptic but requires a ·2 per cent. solution of hydrochloric acid to act in. There are also manufactured solutions containing the pepsin ferment, such as Benger's liquor pepticus, which, like the glycerine extract, are to be added to the ·2 per cent. solution of hydrochloric acid in which the proteid is to be digested.

Fibrin obtained by whipping fresh blood and subsequently washing is the most convenient proteid for experiments in gastric digestion, as, on account of its filamentous structure, the fluid readily permeates it and hence its solution is rapid. More solid substances, such as boiled white of egg, require a longer time for their digestion as the fluid can only penetrate them slowly. Unboiled white of egg and other solutions of proteid undergo the same chemical changes as fibrin, but inasmuch as they are not solids some important physical features of the process of digestion cannot be optically observed. If some strands of fibrin* be placed in a beaker with a plentiful supply of ·2 per cent. solution of hydrochloric acid and a few drops of a solution containing pepsin, such as the glycerine extract or Benger's liquor, be added, and the whole kept at about the temperature of the body, *i.e.*, 35° to 40°C., changes very quickly supervene in the mixture. The fibrin first of all swells up into a transparent jelly which rapidly dissolves, the fluid at the same time becoming turbid, and some granular debris collecting at the bottom of the vessel.

After the fibrin has just passed into solution, more than one kind of proteid is found in the mixture. On boiling it yields no precipitate, so that no proteid coagulable by heat is present, but on neutralisation a precipitate of *acid-albumin* is thrown down—a precipitate soluble in water and dilute acids and alkalies.

* The fibrin may be boiled previous to the experiment in order to kill the small amount of pepsin in it derived from the blood, but in such a case it does not digest quite so quickly.

The solution left after the precipitation of acid-albumin contains still a considerable quantity of proteid matter; a quantity which varies with the length to which the process of digestion has been allowed to go, for the formation of acid-albumin forms the first stage. If the process had been allowed to go far enough there would have been no precipitation on neutralisation at all, the acid-albumin which was first formed having undergone further change.

The remaining neutral solution after the acid-albumin has been removed contains *proteose** and *peptone*, of which the former is the penultimate and the latter the final product of gastric digestion. They may be separated by the addition of ammonium sulphate, when the proteose is thrown down and the peptone remains in solution. The proteose thus obtained gives the usual proteid reactions and like albumin will not diffuse through membranes, or, more properly speaking, only to a small extent; but it differs from it in its non-coagulability by heat. Further, the addition of nitric acid causes a precipitate which disappears on heating and reappears on cooling; and with excess of caustic soda and a trace of copper sulphate proteoses give a rose-pink colouration (biuret reaction). The peptone which is left when the proteose is precipitated by ammonium sulphate resembles its predecessor proteose in not being coagulated by heat, in being soluble in neutral solutions, and in giving the biuret reaction with caustic soda and copper sulphate; but it differs from it and from other proteids in its diffusibility through animal membranes, though its capacity in this way is not equal to that of salts or sugar. As we shall see in dealing with pancreatic digestion later, there are probably more than one kind of proteose and peptone, but we need not consider this at present.

The relative amounts of proteose and peptone present in a gastric digestion mixture depends entirely upon the extent to which digestion has been carried. Proteose represents what we may term the second stage in the transformation of the original proteid, acid-albumin being the first and peptone the last.

It is to be noted that for these results to take place the presence of both pepsin and hydrochloric acid is essential. If hydrochloric acid (·2 per cent. solution) is used alone the fibrin swells up into a jelly, as before, but does not pass on into solution, nor are proteoses and peptones formed; while pepsin in water or in a neutral or

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**Proteose* is frequently called "albumose," but this is scarcely a correct appellation unless it is obtained from albumin. Proteose is the generic name applicable to this substance whatever its source, while *albumose*, *fibrinose*, &c., may be more strictly employed to indicate the source from which it has been obtained.

alkaline solution has no action on fibrin at all. Hydrochloric is, however, not the only acid which in conjunction with pepsin at a suitable temperature will dissolve proteids, though it is the most efficient. Lactic, phosphoric, or sulphuric acid may be substituted, but their potency is not so great. That the acid of the gastric juice is hydrochloric and not an organic acid is shown by the action of the juice on congo-red and methyl-violet, which are differently affected by mineral and organic acids; and, again, when the relative amounts of bases and acid radicals in the juice are estimated quantitatively it is found that there is an excess of Cl—more, that is, than is required to combine with the bases present.

The free acid of the juice is formed, no doubt, from the chlorides of the blood, for when digestion is going on the amount of chlorides in the urine is proportionately diminished; the splitting up taking place in the acid-secreting cells themselves. The following equation suggests the possible change:

$$NaH_2PO_4 + NaCl = Na_2HPO_4 + HCl.$$

The sodium di-hydrogen phosphate having been provided by the action of the CO_2 of the blood upon di-sodium hydrogen phosphate, thus:

$$Na_2HPO_4 + CO_2 + H_2O = NaHCO_3 + NaH_2PO_4$$

The most favourable temperature for gastric digestion is that of the body—about 35° to 40°C. The juice becomes inoperative at 0°C., and on boiling the activity of the pepsin is totally destroyed and can never be recovered. This is in itself in favour of the view that it is a ferment, and there are other reasons for regarding pepsin in this light. While the hydrochloric becomes used up in the process of digestion and requires to be constantly renewed as fresh proteid is added, a small quantity of pepsin will dissolve an indefinite amount of fibrin, provided the products of digestion are removed by dialysis and the supply of hydrochloric acid kept up.

The amount of pepsin present in the juice is extremely small and its exact chemical nature is unknown. Apparently it is not to be regarded as a proteid, but the matter is not yet sufficiently worked out to enable a definite statement to be made. At present our knowledge of the substance amounts to little more than an acquaintance with its powers. According to some it is united with the hydrochloric acid, and they are spoken of as forming a compound substance—*pepsin-hydrochloric acid*. Pepsin does not exist probably as such in the gastric glands, but as a zymogen, to which the name of *pepsinogen* may be given, which is readily converted to pepsin by the action of hydrochloric acid.

In its dependence for its activity on the presence of hydrochloric acid pepsin differs markedly from the ferment ptyalin of the saliva, which, as we saw, was able to act upon starch even in a neutral medium. The change in the proteids under the influence of pepsin and hydrochloric acid seems, however, to resemble that which takes place in starch as the result of salivary digestion, in that it is apparently one of hydration; for if proteids are subjected to the action of strong acids, or of dilute acids and heat, or digested with superheated steam (all of which processes tend to produce a hydrolytic change), they are converted to a form of peptone.

The action of pepsin on proteids other than fibrin is the same, *i.e.*, it converts them to peptone, the ease with which it accomplishes this result varying in different cases. Some substances allied to proteids are, however, totally unaffected by it; and these include mucin, nuclein, and keratin. Gelatine obtained from the gelatigenous element of connective tissue is converted into what may be termed gelatine-peptone, and chondrin and elastin are affected in a somewhat similar manner.

We have yet to consider the action of gastric juice upon milk, in which the second ferment—rennin—is concerned. *Rennin* is commonly obtained from the stomach of the calf, and in its commercial form of "rennet" is largely used in the manufacture of cheese. If milk be subjected to the action of gastric juice at the temperature of the body it clots, and in a little time the clot is digested with the formation, as before, of acid-albumin, proteose and peptone. The clot is due to the precipitation of the proteid *casein* in an insoluble form, entangling fat particles with it much as the fibrin of blood entangles the blood-corpuscles. That the clotting of milk is not due to the presence of the hydrochloric acid alone is shown by the fact that neutralised gastric juice, or an extract containing rennin alone will produce a clot equally well. Rennin, like other ferments of a similar kind, is dependent for its activity on temperature conditions, that of the body being the most favourable, and it is totally destroyed if the solution containing it be boiled. Furthermore, a minute quantity of it will suffice to clot a very considerable amount of casein. It may be separated from the pepsin ferment by the addition of magnesium carbonate to the gastric juice, when a precipitate results which contains the pepsin, the rennin remaining in the clear supernatant fluid after the mixture has been allowed to stand.

Another view that might be taken of the action of gastric juice upon milk—admitting the existence of a milk-curdling ferment—is that the ferment acts by producing lactic acid through

fermentation of sugar of milk; but this is disproved by the fact that if the casein be separated from milk by suitable methods and redissolved so that its solution is entirely free from milk sugar, it may still be precipitated as before by rennin.

When such separated casein is clotted two proteids are said to appear, one of which forms the curd while the other remains in solution; but this clotting depends on the presence of calcic phosphate, and if this salt be absent neither of the proteid products of the action of the ferment passes out of solution. The same splitting up of an original complex substance no doubt takes place in the clotting of milk itself; the original substance being conveniently called *caseinogen*, and of its two products the one forming the curd being *casein* and the one remaining in solution *whey-proteid.*

As acid will itself precipitate caseinogen in milk as a kind of curd, we must suppose that the special action of rennet upon it in some way peculiarly fits it for the further action of the gastric juice, whereby the clot becomes converted, as other forms of proteid do, into acid-albumin, proteose and peptone; but the precise way in which it does so fit it is not at present clear.

One of the most important of the qualities of the gastric juice still remains to be mentioned, viz., that it is highly antiseptic. Just as the inorganised salivary ferment ptyalin is completely destroyed by the pepsin and hydrochloric acid, so are the bacilli of putrefaction which are added to the food in large quantity in the mouth and pharynx. In cases of dyspepsia, when the gastric juice is secreted in too small quantity and frequently almost not at all, putrefactive changes quickly take place in the food after its introduction into the stomach, still further rendering the gastric glands unable to perform their function and leading to the discharge of the gastric contents by vomiting. It is not too much to say that were it not for this antiseptic quality of the juice, whereby the contents of the stomach are kept free from putrefactive influence while undergoing peptonisation and disintegration, gastric digestion would be totally impossible.

We shall have occasion later to review the history of the food in its passage through the alimentary canal as a whole, and at present it will be sufficient to say that in the stomach a considerable portion of the proteid escapes the final change to peptone, some of it being unaffected or in the acid-albumin stage, and some in that of proteose. These portions pass on into the intestine to be further subjected to the action of the pancreatic secretion. The peptone formed in the stomach is absorbed as it is formed, and little, if any, reaches the duodenum. The carbohydrates,

such as starch, glycogen and dextrin, which have not been converted to maltose or dextrose, also pass the sphincter pylori with the fats, cellulose and other indigestible substances, and the constituents of the gastric juice itself; the acid semi-fluid contents of the stomach thus reaching the intestine being known as the "chyme." Peptones, dextrose, salines, water and diffusible substances generally are absorbed into the blood-stream through the mucous membrane of the stomach while digestion is proceeding. Absorption from the stomach, however, is slight as compared with that which takes place in the intestine. The chief use of the stomach is to serve as an antiseptic receptacle for the food, in which it may be prepared for its entrance into the intestine; this preparation taking the form of the further disintegration of the solids by the movements which we shall presently consider, and the conversion to proteoses of the proteids among them, previous to their complete conversion to peptones by the pancreatic juice. The stomach further regulates the amount allowed to enter the intestine at one time: it guards, by the pyloric sphincter, the entrance to the duodenum, allowing only a small portion of the chyme to enter at suitable intervals, so that it may become evenly mixed with the pancreatic juice.

Immunity of the wall of the stomach from the action of the gastric juice.—It may very reasonably be asked, why is the stomach wall not itself dissolved by the secretion of its glands? Though we cannot precisely define the nature of its power of resistance, it is no doubt analogous to that which enables the amœboid cell to dissolve food particles it ingests while its own protoplasm escapes solution. Similarly the epithelium lining the urinary tract is unaffected by its contact with urine, which injuriously affects other tissues, and the fæces which are in almost continuous contact with the epithelial lining of the large intestine have no ill effect upon it, intensely poisonous as they would prove elsewhere. To take yet another instance, a white corpuscle perfectly at home in the plasma of the blood is destroyed if placed in urine or other fluids of the body which are foreign to it. We do not get very much further on the road to answering our question, it is true, by such comparisons, for in none of these cases do we know the cause of the immunity, we can only say that it does exist. It seems to be a rule that certain tissues can withstand the action of certain substances which would be injurious or fatal to the life of other tissues. Thus a secretion is harmless apparently to the cells which secrete it, and to the cells of the duct which conveys it, and to

those lining the surface of the organism on to which it is poured out; and this is obviously a prime necessity physiologically. The other tissues of the body, however, though living, are not necessarily immune. Thus the leg of a living frog introduced into a dog's stomach is digested.

It has been said that the alkalinity of the blood circulating through the vessels of the stomach wall neutralises the acid of the juice, and so prevents its action on the epithelium of the mucosa; but this cannot be regarded as the reason of the immunity for it will not apply to the case of the pancreas, the secretion of which is alkaline, and contains a ferment active in an alkaline medium. As we shall see immediately the pancreatic secretion, alkaline, and a powerful solvent of proteids, has no solvent power over the epithelium lining the intestine, into which it is poured.

Movements of the stomach.—As the stomach becomes distended with food, contractile movements in its wall commence and increase as digestion proceeds. The first movements occur in the wall of the stomach generally, and are of a somewhat rhythmical peristaltic nature, and lead to a *churning up* of the gastric contents, whereby they are converted into a more fluid form and thoroughly mixed with the gastric juice. Otherwise considerable portions of the food would escape admixture with the juice, and be deprived of the benefit of its peptonising and antiseptic qualities. But shortly after digestion has commenced, movements of a more definite kind supervene, the end of which is to propel portions of the chyme from time to time into the intestine, and these may be termed, therefore, movements of *propulsion.* They commence in the region of the circular fibres marking the commencement of the antrum pylori, and extend towards the pylorus itself, the sphincter pylori relaxing from time to time to allow of the passage of some of the chyme through it. The action of the sphincter, however, is affected by the character of the food sent against it by this propulsive movement, for the impact of solid portions tends to make it contract, and they are thus prevented from entering the duodenum, and returned to the general maelstrom of the stomach to be again churned up with the more fluid contents. According to some authorities, however, the fundus has little or nothing to do with either the churning or propulsive movements, which are carried on entirely by the pyloric portion of the stomach, the cardiac portion acting merely as a reservoir.

The precise way in which the food causes the contractions of the stomach wall is not quite clear. The contractions are not

proportional to the distension, for in the early stages of digestion, when the stomach contains more food than in the later, they are much less vigorous. It is possible that they may be influenced by the absorption of the products of digestion; or the degree of their intensity may have some relation to the activity of the gastric contents, which increases as digestion proceeds. But these are merely hypotheses. The rationale, both of secretion of the gastric follicles and of the movements of the gastric walls, is no doubt complicated, and the precise causes and their *modus operandi* have not yet been fully determined.

Before leaving the consideration of the movements of the stomach, a few words may be said as to the muscular and nervous mechanism of the act of **vomiting**, whereby the gastric contents are propelled upwards instead of downwards (*i.e.*, in the opposite direction to the normal one), and ejected through the mouth. Vomiting usually results from irritation of the gastric wall by the presence of undigested food, and is then a reflex act in which many muscles and nerves are concerned. It is usually preceded by a feeling of nausea, and ushered in by a copious flow of saliva. The diaphragm is pressed down upon the abdominal viscera by a deep inspiration, the glottis being then closed, in order to keep the muscle in the inspiratory position. This is succeeded by a forcible contraction of the abdominal muscles of the wall of the stomach itself, and by a relaxation or dilation of its cardiac orifice. Under the influence of these forces the food is pressed out of the stomach, along the œsophagus, and usually through the mouth alone to the exterior, the nasal chamber being shut off by the approximation of the posterior pillars of the fauces.

Some writers consider that the stomach wall itself does not take part in the process (does not contract), only the diaphragm and abdominal muscles by their contraction being responsible for the pressure on the gastric contents. One might, however, expect *a priori* that the stomach would itself contract to secure more complete evacuation, and there seems to be some reason for supposing that it actually does do so. Division of the vagi, which one would regard as the efferent motor nerves to the stomach wall, renders vomiting difficult, and this would certainly lead us to think that the difficulty is the result of impulses no longer passing down these nerves. Again, a case is recorded in which the abdominal muscles were paralysed by injury to the spinal cord above the origin of their nerves, and yet vomiting could be brought about. Further, in young children the stomach alone seems to be efficient in producing the act. But though the stomach probably takes its share of the work, its action does not

appear to be essential, for if it be replaced by a bladder containing fluid, vomiting may still be induced. Perhaps in ordinary vomiting the abdominal muscles and the diaphragm initiate the movement, and perform the heaviest part of the work, which is the more completely carried out through the ensuing contraction of the gastric wall itself.

Nervous mechanism of vomiting.—We have seen that vomiting usually results from irritation of the gastric branches of the vagus, which are thus the afferent nerves in a reflex act, but the impulse may reach the medulla along other nervous paths. Thus tickling the fauces, the soft palate, the root of the tongue and the pharynx will produce vomiting from stimulation of the glosso-pharyngeal—the sensory nerve of these parts; and the insertion of the finger into the throat is a frequent and practical method of inducing the act. Irritation of other parts of the alimentary canal has a similar power of inducing vomiting, as shown in cases of ligature of the intestine or hernia, the mesenteric nerves carrying the afferent impulse. Though stimulation of some part of the alimentary canal is the most frequent cause of vomiting, irritation of other organs may induce it. It is not infrequent in phthisis, from irritation of the branches of the vagus nerve to the pulmonary tissue, and in cases of renal calculus the nerves of the urinary apparatus convey the afferent impulse. Irritation of the vagus branches to the liver and gall duct, of the uterine nerves in pregnancy, and of the nerves to the ovary or testicle when these organs are inflamed, frequently causes reflex vomiting. Any of the nervous tracts indicated above may thus convey the impulse to the centre in the medulla, whence it is reflected outwards by the phrenic nerves to the diaphragm, the vagus to the œsophagus and stomach, and the intercostals to the abdominal muscles.

But though vomiting is thus usually a reflex act resulting from some peripheral stimulation, it may be more central in its origin, as when it results from disease of the cerebrum or cerebellum or even of the medulla itself. Similarly the thought, sight, or smell of anything particularly disagreeable may cause it, the impulse arising then in a higher part of the brain and passing downwards to the medullary centre. Finally, vomiting may be a purely voluntary act, the capacity for which varies in different people. Some cannot by any voluntary effort induce it without peripheral stimulation, *e.g.*, of the fauces; others seem to have the power of evacuating the stomach at will, a faculty requiring some practice for its attainment, and more common among dyspeptics than others.

Drugs ("emetics") eapable of indueing vomiting may act in either of two ways—(1) By irritation of some afferent surfaee, such as the gastric mueosa; of these zinc sulphate may be taken as an example. (2) By acting upon the vomiting eentre itself, as in the ease of apomorphia, whieh is injected subeutaneously.

CHAPTER IX.

ALIMENTATION (continued).

Digestion in the Intestine.

WHEN the chyme escapes from the stomach through the pylorus it enters the intestine, and in its passage along the remaining part of the alimentary canal it becomes mixed with the pancreatic and intestinal juices and the bile. Of these the most important in its action upon the food is the secretion of the pancreas; and the liver, as we shall see later, has other functions than the production of bile, which is mainly, if not entirely, an excretory product.

The **structure of the intestine.**—The intestine as a whole extends from the pyloric end of the stomach to the anus, and is anatomically divisible into two main subdivisions—the *small* and *large intestine*, so named from the relative diameters of the lumen in these two parts.

The **small intestine** extends from the pylorus to the *ileo-cœcal valve*, where it joins the larger gut, and is some 20 feet in length. The first eight or ten inches below the pylorus is called the *duodenum*, the upper two-fifths of the remainder the *jejunum*, and the lower three-fifths the *ileum*.

The small intestine resembles the stomach in the possession of four coats—mucous, submucous, muscular and peritoneal. The structure of the peritoneal investment is the same as it is in the case of the stomach and elsewhere, and needs no special mention. The muscular coat consists of two layers—internal circular and external longitudinal—both composed of bundles of non-striped muscle fibres supported by connective tissue. Between the layers lies a well-marked plexus of non-medullated nerve-fibres with ganglion cells placed at the nodes of the meshwork—*Auerbach's plexus*, as it is termed. Within the muscular coat is the submucous, consisting of loose connective tissue containing blood-vessels, lymphatics, and nerves; in the duodenum the alveoli of

Brunner's glands, to be shortly described; and in some parts *Peyer's patches* and *solitary follicles*. It also contains a special plexus of nerve-fibres similar to Auerbach's, but with more delicate strands, called *Meissner's plexus*.

The mucous coat is the most important layer of the intestinal wall, as it contains the secretory glands and presents other noticeable features, chief among which being the villi projecting from its inner surface. On first examining the interior of the gut with the naked eye, it will be seen that the lining membrane—*the mucosa*—is raised up along a great part of its course into transverse folds, which are termed the *valvulæ conniventes*, and extend round one-half or two-thirds of the tube. They commence an inch or two below the pylorus, and extend through the jejunum and into the ileum, about the middle of which they cease. They consist of a doubling inwards of the whole mucous membrane, including the muscularis mucosæ, a thin sheet of submucous tissue forming the core of the fold; and, unlike the rugæ of the stomach, the folds are permanent and do not disappear on distension of the tube. Their purpose is to afford an increased surface for the glandular epithelium covering them.

When the lining of the small intestine is examined still more closely it is seen to present a velvetty appearance, due to the presence of numerous processes on its surface, termed *villi*, which are about $\frac{1}{2}$ to 3 mm. in length, and set closely together, and found in every part of the tube. Under the microscope, the structure of the mucosa bears a family resemblance to that of the stomach, but presents some remarkable differences. Separating it from the submucous layer is the *muscularis muscosæ*, here, as in the stomach, consisting of two layers of non-striped muscle-fibres—an internal circular and an external longitudinal—and here, as in the stomach, sending processes into the mucosa itself, the destiny of which we shall see immediately. The epithelial lining of the intestine, continuous with that of the stomach, is glandular, and in a single layer which is repeatedly involuted to form a series of glands. These are termed the *glands of Lieberkühn,* and they are continuous with those of the pylorus, though differing somewhat in their anatomical characters. They are simple test-tubes, placed side by side vertically to the muscularis mucosæ, and show no division into a mouth or duct and a fundus. They thus form an example of the earliest stage of gland development—they are simple tubular glands. The cells lining them are similar to the chief cells of the cardiac glands and those lining the secretory part of the pyloric glands—short columnar, finely granular cells with a nucleus in their basal third. Here and there one of the

cells may be seen to have become a goblet cell. As the epithelium is followed upwards through the outlet of the gland, it is found to be more columnar where it covers the ridge between the two tubules, and forms the lining proper of the intestinal canal itself. Usually, however, on thus following the epithelium of a Lieberkühn's follicle upwards, it will be found not to turn over a ridge between it and a neighbouring follicle but to become continuous with the columnar epithelium covering a villus, the base of which corresponds with the level of the opening of the gland; and if the epithelium of the villus be followed up the one side of it and down the other it will be found frequently to become continuous with the cells lining a test-tube gland placed on the other side. In other words, the continuity of the epithelial lining of the intestine is unbroken throughout; in some cases it is pushed outwards to form the test-tube glands, and again in others it is pushed inwards to form the covering of the villi, but it always exists as an uninterrupted sheet, as is shown in a somewhat painfully diagrammatic manner in Fig. 246.

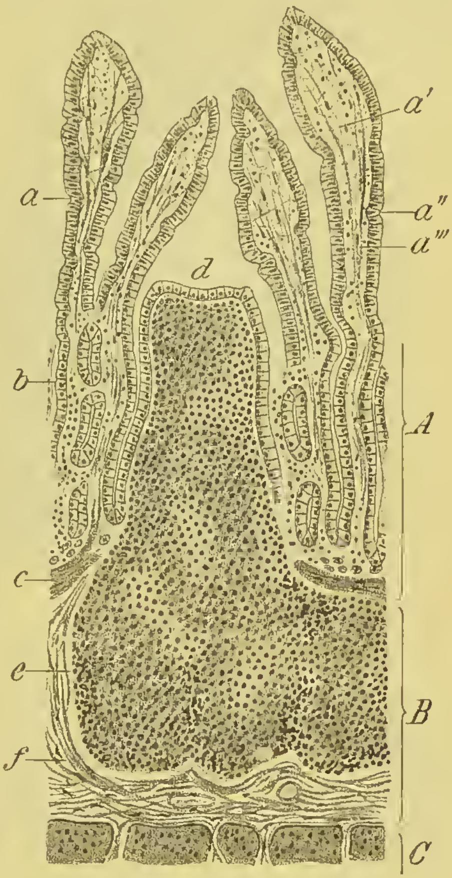

Fig. 245.—Vertical Section of small Intestine of Cat, through Peyer's Patch.

A, Mucosa; *B*, submucosa; *C*, muscular coat; *a*, villus; *a'*, central lacteal; *a''*, Watney's node; *a'''*, strands of muscle-fibres from muscularis mucosæ; *b*, Lieberkühn's follicle; *c*, muscularis mucosæ, giving off strands to villi; *d*, epithelium, covering *e*, lymph-follicle of Peyer's patch; *f*, connective tissue of submucosa.

The epithelium where it covers the villi differs considerably from that of Lieberkühn's follicles. It consists of a single layer of tall columnar cells, placed palisade-wise upon a basement membrane. The cells have a striated hem at their broader, free ends, and an oval nucleus in their basal third, its long axis in that of the cell. The striated hem of the cells

placed in series stands out in sections as a bright refractile border to the epithelial covering as a whole. Here and there some of the columnar cells may be seen to have become converted to goblet mucin-forming cells. Between the narrower basal portions of the columnar cells leucocytes may sometimes be seen which have evidently migrated from the meshes of the adenoid tissue within the villus.

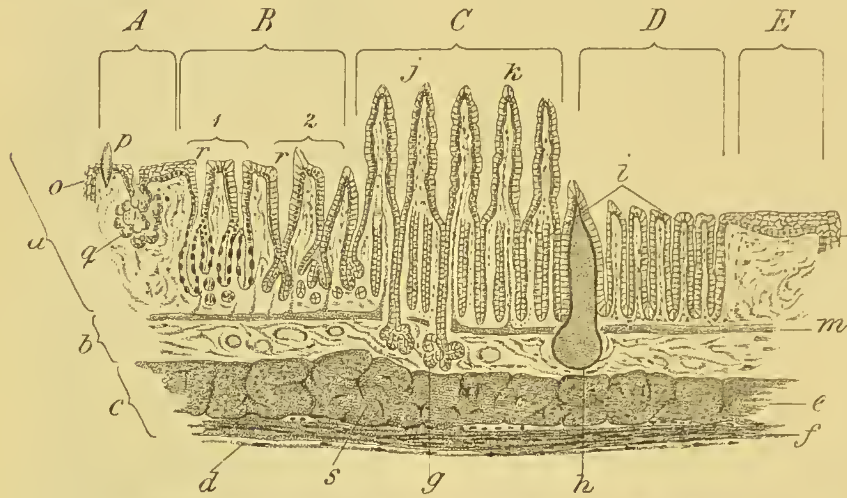

Fig. 246.—Diagrammatic representation of Wall of Alimentary Canal.

A, mouth and œsophagus; *B*, stomach—1, cardiac end, 2, pyloric end; *a*, mucosa; *b*, submucosa; *c*, muscular coat; *d*, peritoneal coat; *e*, internal circular muscular coat; *f*, external longitudinal muscular coat; *g*, glands of Brunner; *h*, solitary gland; *C*, small intestine; *D*, large intestine; *E*, rectum; *j*, villi of duodenum; *k*, villi of jejunum and ileum; *i*, glands of Lieberkühn; *m*, muscularis mucosæ; *n*, skin beyond anus; *o*, skin beyond mouth; *p*, tooth; *q*, salivary gland; *r*, mouths of gastric follicles; *s*, pyloric sphincter.

The epithelium of the villi and of Lieberkühn's glands rests upon a basement membrane formed by a surface condensation of the delicate, somewhat adenoid tissue beneath it, which fills the space between the epithelial layer and the muscularis mucosæ and supports the structures found in it. In the deeper part of the mucosa the adenoid reticulum surrounds and separates from each other the individual gland tubules, and is permeated by a capillary network, and traversed by strands of fibres from the muscularis mucosæ on their way to form part of the cores of the villi. The *core of the villus* contains in the centre a *lacteal* vessel ending blindly, its walls formed of a layer of flattened epithelial cells with sinuous outlines. This lacteal or lymphatic capillary is continuous with lymphatics placed more deeply in the

mucosa, and, as we shall see, receives the fat absorbed by the epithelium covering the villus and transmits it through the mesenteric lymphatics to the receptaculum chyli of the thoracic duct. Between the central lacteal and the epithelium of the villus, or rather the basement membrane on which the epithelium rests, is found the retiform or adenoid tissue already mentioned, traversed by blood-vessels and non-striped muscle-fibres, both of which are continuous with similar structures in the deeper parts of the mucosa. The blood-vessels are represented by a small artery (a continuation of one derived from the larger branches in the submucosa, which has penetrated the muscularis mucosæ and passed inwards between the glands of Lieberkühn) which runs up on one side of the villus, breaking up into capillaries as it goes, and one or two corresponding veins which receive the blood from the capillary network, and passing down the other side traverse the mucosa, and piercing the muscularis mucosæ join the larger venous trunks in the submucosa (Fig. 248).

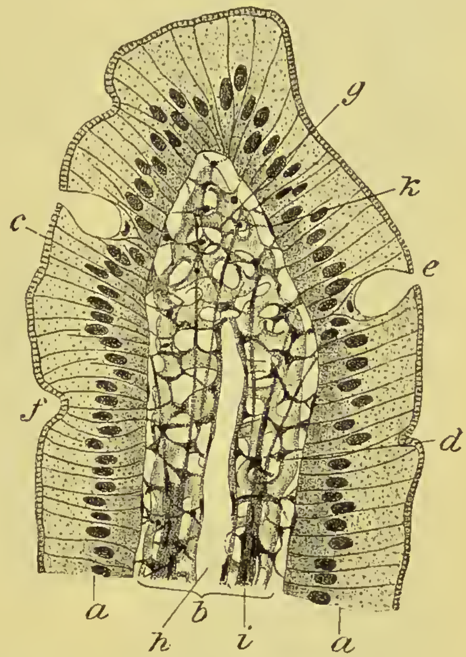

Fig. 247.—Vertical Section of Villus of Cat's Intestine.

a, Layer of columnar epithelial cells; *b*, interior of villus; *c*, striated hem of epithelial cells; *d*, adenoid reticulum; *e*, mucous cell; *f*, Watney's node; *g*, network of capillaries filled with injection; *h*, central lacteal of villus, *i*, strand of non-striped muscle-fibres; *k*, nuclei of basement membrane.

The muscular fibres in the villus belong to delicate strands derived from the muscularis mucosæ, and spread out towards their termination to be inserted into the basement membrane—the surface condensation of the connective tissue basis of the villus. By their contraction they periodically shorten the villi during the process of absorption.

Brunner's glands occur at the commencement of the duodenum, immediately below the pylorus of the stomach. They are compound tubular glands, and their acini lie in the submucous coat, their long ducts piercing the muscularis mucosæ to open between

the villi; or we may say that the duct of one of these glands, after piercing the muscularis mucosæ, opens into the lower extremity of a Lieberkühn's follicle. The alveoli are lined by short columnar cells similar to those of the secretory portion of the pyloric glands of the stomach.

Peyer's patches and solitary follicles.—Solitary follicles occur both in the large and small intestine, and in the latter they are frequently collected into groups, which are termed Peyer's patches. These are aggregations of lymphoid nodules, from one to three

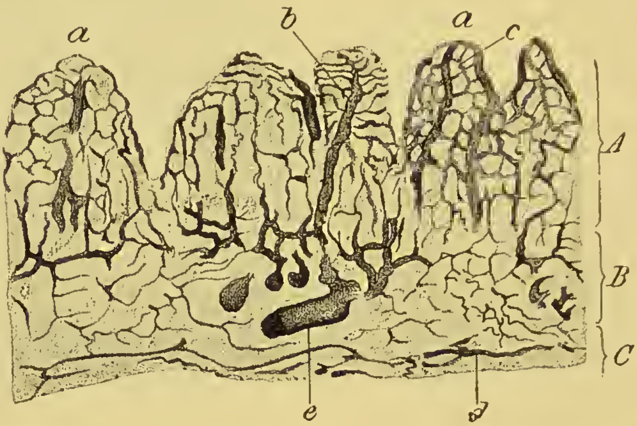

Fig. 248.—Vertical Section of Small Intestine of Rabbit.

A, Mucosa; *B*, submucosa; *C*, muscular coat; *a*, injected villi; *b*, artery or vein of villus; *c*, capillary network of villus; *d*, vessels of muscular coat; *e*, large vessel in submucosa.

inches in length and about half an inch in width, the long axis of the patch being in that of the intestine itself; and they are placed opposite the attachment of the mesentery. One of the solitary follicles of which a Peyer's patch is composed consists of a reticulum of adenoid tissue containing numerous lymph-corpuscles, the whole being surrounded by a lymph space in communication with neighbouring lymphatics. An afferent artery enters the adenoid tissue and breaks up into a capillary network, from which the blood is collected and returned to the deeper parts by an efferent vein. The follicles have their base in the submucosa, and project through the muscularis mucosæ (Fig. 245) against the epithelium lining the intestine, at the level of the opening of Lieberkühn's follicles, and are covered only, therefore, by a single layer of short columnar cells separating them from the lumen of the gut itself. Solitary follicles are found scattered throughout the small intestine, Peyer's patches being most numerous in the lower part of the ileum, and, as already stated, they are placed opposite its mesenteric attachment. No Peyer's patches occur in

the large intestine, but only solitary follicles, which are found in the submucosa, especially in the cæcum and vermiform appendix.

The **large intestine**, from four to six feet long, is subdivided into the *cæcum*, the *colon* (ascending, transverse and descending) and the *rectum.* The *ileo-cæcal valve* separates the ileum from the cæcum, and from the latter projects the *vermiform appendix.* The large intestine differs from the small in possessing no villi, and the muscular coat is differently arranged. The external longitudinal layer of fibres in the cæcum and colon is gathered into three strong bands instead of forming a uniform investment to the tube, and these being shorter longitudinally than the rest of the gut draw it up into folds, which form sacculi in the intervals between them. In the rectum, however, this peculiar disposition of the external muscular layer disappears, the bands again spreading out, and in this situation forming a thicker covering than in any other part of the canal. At the lower end of the rectum the internal circular fibres are increased in number and form the internal sphincter of the anus.

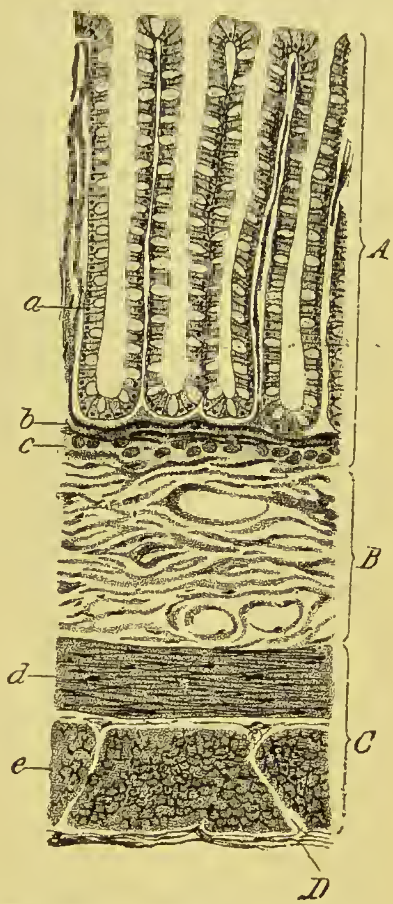

Fig. 249.—Vertical Section of Large Intestine of Cat.

A, Mucosa; *B*, submucosa; *C*, muscular coat; *D*, peritoneal coat; *a*, Lieberkühn's follicle; *b*, inner layer of muscularis mucosæ; *c*, outer layer of muscularis mucosæ; *d*, inner circular division of muscular coat; *e*, outer lougitudinal division of muscular coat.

The mucosa, as already stated, possesses no villi, nor is it thrown into folds to form valvulæ conniventes. It consists mainly of Lieberkühn's glands placed side by side, with a little connective tissue supporting blood-vessels between them. These glands are larger than the corresponding ones in the small intestine, with a wider lumen, and the mucous or goblet cells are much more numerous among the ordinary short columnar ones.

Nodules of lymphoid tissue—solitary glands—are to be found in the submucous coat, and especially in the cæcum and vermiform appendix.

The ileo-cæcal valve is represented by two opposing folds of mucous membrane projected inwards from the wall of the gut at the junction of the ileum and cæcum, the projection being towards the latter and away from the former. When the contents of the cæcum press against them, they are thus brought into opposition, and prevent regurgitation into the ileum. In this way the folds act as an ordinary valve, allowing the intestinal contents to pass only in one direction. They are strengthened by muscular fibres from the circular coat, which lie between the two sheets of mucosa forming each valvular fold. The surface of the folds directed towards the ileum bears villi, that towards the cæcum none.

The same plexuses of nerve-fibres are found in the muscular and submucous coats of the large intestine as in the small.

The epithelial lining of the *rectum* resembles that of the rest of the large intestine. The mucous membrane of this part of the canal is thrown into numerous folds when it is empty, which disappear when it becomes distended, in this way resembling the mucosa of the œsophagus and stomach.

Of the structures described above, the glands of Lieberkühn in the small and large intestine secrete the *succus entericus*, or intestinal juice, with which the food becomes mingled in passing through these parts of the alimentary canal; and these glands, as we have seen, are scattered uniformly throughout the lining membrane of the canal itself, and are of very simple construction. But the pancreas and the liver, which also contribute their secretion to the total of the intestinal contents, are much more complicated structures, which in the course of development have receded from immediate connection with the alimentary wall, with which they are only associated through their ducts. Nevertheless, they are essentially merely out-pushings from the hypoblastic epithelial lining, just as Lieberkühn's follicles are, but out-pushings which have undergone further development and elaboration.

Structure of the pancreas.—The **pancreas** is a compound racemose gland, very similar in the general arrangement of its parts to the salivary glands. It consists of ducts and alveoli, supported by connective tissue containing blood-vessels, nerves and lymphatics, which affords a general investment, too, for the whole organ. From the inner surface of the capsule septa pass into the substance of the gland, dividing it into lobes and lobules. The several interlobular ducts are gathered together to form one main one running longitudinally, which in man opens into the duodenum at the same point as the bile duct. In the rabbit the duct of the pancreas opens separately into the intestine at a

lower level than the bile duct. Of the intra-glandular branches of the duct it need only be said that in the main they are similar in character and disposition to those of the salivary glands; but the striation of the columnar cells in the larger ducts is not so marked, and the intermediate ducts or ductules lined with flattened cells are longer.

The alveoli are tubular, more distinctly so than those of the salivary glands, and their lumen is surrounded by cells of the serous type, columnar or wedge-shaped, with a nucleus a little outside their middle. The cells rest on a basement membrane, which is continued in a less distinct form along the ducts.

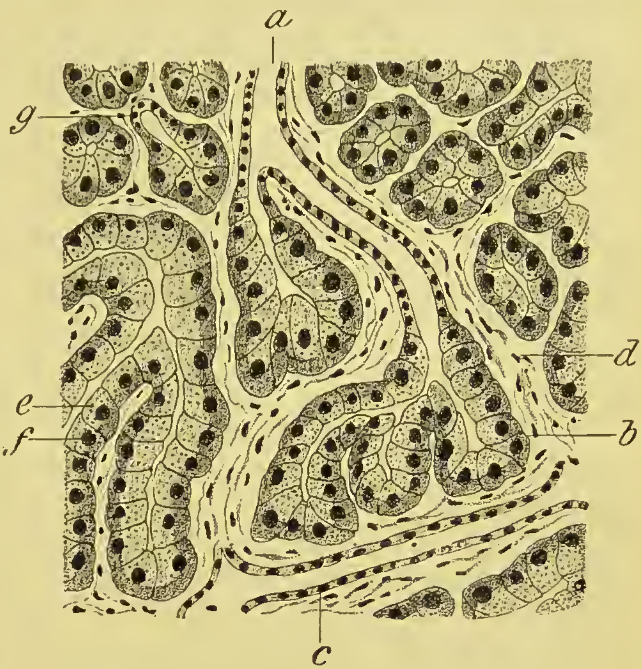

Fig. 250.—SECTION OF PANCREAS OF DOG.

a, Intermediate duct; *b*, terminal alveoli; *c*, another intermediate duct; *d*, fibrous tissue septum; *e*, lightly-stained central part of cell; *f*, deeply-stained peripheral part of cell; *g*, intermediate duct, cut across as it issues from alveolus.

In the alveolar cells, more distinctly than in those of the parotid, two zones may be differentiated—an outer, purely protoplasmic one and an inner containing secretory granules (the precursors of some of the most important constituents of the pancreatic juice); and here, more distinctly than in other glands, the differences between the loaded and exhausted conditions may be made out. If the gland has not been secreting, as when the animal has been without food for some considerable time, the non-staining secretory granules are increased in number, and may extend almost, if not entirely, throughout the cell, the outer, purely protoplasmic zone being proportionately reduced. On the other hand, after continued activity, as when the animal has been fed a few hours before, it is found that the secretory granules have been discharged into the lumen of the tube: the breadth of the inner zone being thus decreased as the outermost granules move inwards

to replace those which are thus lost. Finally, only a narrow ring of granules surrounds the lumen, the outer protoplasmic zone being proportionately increased in depth.

Furthermore, after secretion the cells are comparatively small and shrunken, their outlines more defined, and their nuclei, which the granules obscured, stand out clearly. The lumen of the tube, which in the loaded state of the cells is small and indistinct, becomes more appreciable, and the outer contour, instead of being even, is irregular, being indented at the margins of the cells. The discharged cell stains more deeply than the resting one, from the removal of the non-staining granules, and the condensation of the readily staining protoplasm.

Accompanying these differences are alterations in the calibre of the blood-vessels, which dilate when the gland commences to secrete, and so provide it with an increased supply of blood.

"These several observations suggest the conclusion that in the gland at rest the cell is occupied in forming, by means of the metabolism of its cell substance, and lodging in itself certain granules of peculiar substance, intended to be a part, and probably an important part, of the secretion. This goes on until the cell is more or less completely 'loaded.' In such a cell the amount of actual living cell-substance is relatively small, its place is largely occupied by granules, and it itself has been partly consumed in forming the granules. During the act of secretion the granules are discharged to form part of the secretion, other matters, including water, making up the whole secretion; and the cell would be proportionately reduced in size were it not that the act of discharge seems to stimulate the cell-substance to a new activity of growth, so that new cell-substance is formed; this, however, is in turn soon in part consumed in order to form new granules. And what is thus seen with considerable distinctness and ease in the pancreas is seen with more or less distinctness in other glands" (Foster).

Before leaving the consideration of the structure of the pancreas, it must be mentioned that in addition to the alveoli of the gland there are to be found here and there small collections of epithelial-like cells, rounded or polyhedral in shape, with well-defined nuclei. Each of the islets is supplied with a network of capillaries. Their function is at present unknown, though many believe that they form an internal *secretion* presiding over carbohydrate metabolism.

In the centre of the alveoli—*i.e.*, in the lumen of the tubules—small spindle-shaped cells are sometimes to be seen, which have been termed from their position *centro-acinal.*

The **pancreatic juice.**—The secretion of the pancreas, which is poured into the duodenum through the orifice common to it and the liver, is clear, viscid, and alkaline in reaction. Its specific gravity is about 1030, and thus considerably higher than that of the gastric juice or the saliva. The following is said to represent the proportion of water and solids in man :—

$$\begin{array}{lll} \text{Water} & 97{\cdot}6 \text{ per cent.} & \\ \text{Solids} & \underline{2{\cdot}4} \text{ per cent.} & \left\{\begin{array}{l} 1{\cdot}8 \text{ organic.} \\ {\cdot}6 \text{ inorganic.} \end{array}\right. \\ & 100 & \end{array}$$

But the relative amount of solids and water varies with the rate of secretion, the more rapid the secretion the greater proportionate amount of fluid to solid. The juice may be obtained from animals by means of either a temporary or permanent fistulous opening into the pancreatic duct; but when the opening is a permanent one the character of the secretion undergoes alteration, and the proportion of water to solids rises. In the dog the amount of solids in the juice obtained from a temporary fistula is about 8 or 10 per cent. Of this, some nine-tenths consists of proteids, and nearly one-tenth of inorganic substances, mainly sodium carbonate with some sodium chloride. Traces of fats, soaps, and sometimes leucin may be present. The proteids consist of albumin, which coagulates on heating, and some proteid allied to myosin, which enables the juice to clot spontaneously. Furthermore, four ferments are recognisable by their action upon foodstuffs :—

1. A peptone-forming ferment (*trypsin*).
2. A sugar-forming ferment (*amylopsin*).
3. A fat-splitting ferment (*steapsin*).
4. A milk-curdling ferment.

Origin of the secretion.—With all the secretions already studied, the activity of the cells has been brought about through the reception of afferent impulses derived from the presence of food material in some part of the alimentary canal, and while it is possible that this is to a certain degree the case also with the pancreas, it is certainly by no means the most important, for the secretion takes place in the usual way after all the nerves are divided. The nervous supply of the gland has been very fully studied by Pawlow. He found that stimulation of the vagus (after special precautions had been taken to eliminate the action of the cardio-inhibitory fibres of the nerve) produced a copious formation of the juice, though the latent period was very pronounced compared with the other glands, and that the secretion

depended to a great extent on the vascular supply, for if the constrictor fibres were stimulated so that the blood flow to the gland was diminished, the flow was at once arrested. He also found that if the other vagus was stimulated while the secretion was taking place it was at once arrested, so that we may infer that the nerve contains both secreto-motor and secreto-inhibitor fibres. During the past few years, however, it has been shown that another factor is concerned in the production of the juice of apparently greater importance than the reflex arc just described, for, as I have said, secretion continues after all the nerves have been divided if an acid solution be introduced into the lumen of the duodenum, and it is now known that if a faintly-acid extract be made of the mucous membrane of this portion of the bowel and injected into the blood a very pronounced secretion at once results. It is now supposed that a certain body called pro-secretin is formed by the epithelial cells and transformed into secretin through the influence of the acid in the gastric juice contained in the chyme as it passes into the duodenum. The pro-secretin can be obtained readily from the mucous membrane of the upper part of the gut by extracting with saline, but if this be injected no effect is noticed on the activity of the gland, though if this extract be boiled or acidified it at once becomes active. The chemical nature of secretin is unknown.

Stimulation of the medulla will also cause secretion by the pancreas, and the secretion is not arrested by section of the vagi. This has been taken as a proof that the vagi are not secretory nerves for the gland, but it cannot justly be so regarded. It certainly, however, may be considered an indication that other nervous tracts (*e.g.*, the sympathetic) probably transmit efferent secretory impulses to it, and this is supported by the fact that stimulation of the spinal cord will also cause the pancreas to secrete or to increase its secretion.

Stimulation of the central cut end of the vagus will reflexly inhibit the secretion of pancreatic juice, and in the act of vomiting this is no doubt the path by which the inhibitory impulse travels; but the vagus doubtless acts here merely as any other sensory nerve will, the pancreas being very sensitive to any external condition.

In man the amount of pancreatic secretion per diem is said to be from 200 to 300 c.c.

The pressure in the pancreatic duct never rises, as it may in the ducts of the salivary glands. If a cannula be introduced into the pancreatic duct of a rabbit and connected with a manometer the pressure does not exceed about 17 mm., the gland at this point becoming œdematous.

When the nerves which reach the pancreas from the solar plexus are divided, "paralytic" secretion of a thin and watery character results.

We may now consider in greater detail the action of the juice on the constituents of the food.

1. *Action upon proteids.*—Pancreatic juice may be obtained, like gastric juice, through a fistulous opening, the linea alba being incised and a cannula introduced into the pancreatic duct. Needless to say, however, for ordinary laboratory purposes so troublesome a method is not employed, an extract containing the ferments being used instead. A glycerine extract may be made of the gland twenty-four hours after removal from the body, which in a 1 per cent. solution of sodium carbonate has strong proteolytic properties; or Benger's liquor pancreaticus may be similarly used. If, however, a perfectly fresh pancreas—one warm from the body—be extracted with glycerine, it is found that it is almost inert towards proteids, even in a 1 per cent. solution of Na_2CO_3, in other words, that it contains little or no trypsin. But if the extract be diluted with water and kept for some time at the body temperature it becomes active, and more quickly so if slightly acidulated water be employed. From this it is apparent that the living pancreas when loaded and about to secrete, or even during the act of secretion itself, contains in its gland-cells little or no trypsin, which seems to result from the decomposition of some precursor or mother-substance. When the gland secretes this, decomposition takes place, and the granules of the mother-substance, or *trypsinogen*, as it may conveniently be termed, split up with the formation of the ferment trypsin as one of the products of their decomposition. Similarly, when the gland is removed from the body and kept for some hours before being treated with glycerine, the same decomposition of trypsinogen takes place, and an extract made after this lapse of time is consequently proteolytic; and an extract of perfectly fresh pancreas, as we have seen, will, if it be diluted with water and kept for some time at a suitable temperature, develop the same powers. This precursor—trypsinogen—therefore belongs to the class of *zymogens* or *mother ferments;* and no doubt the chief cells of the gastric glands contain a corresponding *pepsinogen*, which bears a similar relation to the pepsin of the gastric juice.

The trypsinogen is probably contained in the granules in the inner zone of the pancreatic cells, for the amount obtainable from a gland varies with the depth of the zone; and the other organic constituents of the juice doubtless are derived from these same granules.

If a few shreds of fibrin be placed in a beaker containing a 1 per cent. solution of sodium carbonate and a few drops of pancreatic extract be added, the mixture being kept at a temperature of 35°C., the fibrin soon becomes dissolved, a granular residue collecting at the bottom of the vessel. It does not, however, previously swell up, as we saw it did in the case of gastric digestion, but rather becomes corroded, *i.e.*, eaten away from the surface inwards. On filtering, the filtrate is found to contain alkali-albumin, albumose (proteose), and peptone, and if the process has been carried far enough leucin, tyrosin, aspartic acid, &c., leucin being amido-caproic acid of the fatty acid series, while tyrosin is a phenyl compound of amido-propionic acid. In pancreatic digestion, therefore, as contrasted with peptic, the action does not stop with the formation of peptone, but some of the latter is carried a step further on the road of hydrolysis, with the formation of such products as leucin and tyrosin.

But we have now to note that however far the action of the trypsin ferment is carried, only about one-half of the peptones formed undergo the further change, and this very important fact has been explained by the theory that each molecule of albumin (or fibrin) contains two elements, one of which resists the change while the other suffers it. Thus when fibrin is acted upon by peptic or tryptic digestive fluid, it is converted to antipeptone and hemipeptone, each of which has its precedent antialbumose or hemialbumose and in ordinary peptic digestion the peptone stage is the last reached. But trypsin, which is in every way a more powerfully hydrolytic agent than pepsin, acts further upon the hemipeptone, splitting it up into leucin, tyrosin, &c., while it has no further influence on the antipeptone. The action of the two ferments on this assumption may be expressed in the following table, thus :—

Albumin.

Antialbumose. Hemialbumose.

Action of Pepsin or Trypsin. { Antipeptone. Antipeptone. Hemipeptone. Hemipeptone.

Leucin. Tyrosin. Leucin. Tyrosin. } Special action of Trypsin.

It will be noted that, as in the hydrolysis of starch, the resulting products are always doubled.

When putrefactive changes are not excluded, as they usually are by the addition of thymol to the mixture, other changes take

place in it, due to the action of putrefactive organisms, and indol, skatol, &c., appear, giving rise to a fæcal odour; but this has nothing to do with pancreatic digestion proper.

We have seen that whereas pepsin requires for its activity an acid medium, trypsin acts vigorously in an alkaline one, but it is not nearly so dependent on the reaction of the fluid in which it works as pepsin is. Thus it will act to some extent in a neutral solution, and even in the presence of dilute hydrochloric acid of the strength of ·012 per cent.; but a strength of ·1 per cent. destroys it.

That it is essential that the proteolytic ferment of the pancreas should possess this comparative indifference to reaction is shown by the varying reaction of the intestinal contents. Thus as the food leaves the stomach it is of course acid, and it may remain so till the lower part of the gut is reached, as it has been found to do in dogs, in which it was faintly acid throughout. In man and omniverous animals, with whom vegetables form a constant constituent of an ordinary diet, lactic and butyric fermentation is always liable to occur, and acidity is thereby the more likely. On the other hand, the entrance of the alkaline bile and pancreatic juice into the duodenum may more than neutralise the acidity of the chyme, and in the duodenum at all events the reaction may be alkaline while the secretion of bile and pancreatic juice is at its height. It will thus be seen that the reaction of the intestinal contents varies with the food taken, the changes it undergoes, and other circumstances—it varies from time to time in the same individual—and trypsin to be effective must be in some measure independent of it.

Nuclein and elastin are both dissolved by trypsin, and, unlike pepsin, it will digest mucin.

Of the albumoses and peptones formed during the digestion of proteids, either by peptic or tryptic fluid, several forms have been distinguished. Thus hemialbumose has been found by some to consist of—(1) protoalbumose, (2) deuteroalbumose, (3) hetero-albumose, and (4) dysalbumose, each of which has its characteristic reaction distinguishing it from the rest. There is, again, antipeptone, hemipeptone, and amphopeptone, the latter being the mixture of the first two obtained by the action of pepsin on proteids. For the reactions and chemical characters of albumoses and peptones generally see page 6.

2. *Action upon milk.*—The pancreatic juice will curdle milk, but we do not know the precise purpose of the milk-curdling ferment, as the milk has already been curdled by the gastric juice.

3. *Action upon starch.*—The pancreatic juice, like the saliva, converts starch to a mixture of dextrin and maltose by the action

of the ferment *amylopsin.* It acts more vigorously, however, than ptyalin, readily dissolving unboiled starch, and the maltose is carried a step further and converted to dextrose if the action is prolonged.

4. *Action on fats.*—The action on fats is two-fold. In the first place it emulsifies fats, partly in virtue of its alkalinity and partly through the presence of albumin in it in some quantity. This emulsification, by which is meant the suspension of the fatty particles in a finer state of subdivision, must be distinguished from the second action, that of splitting fats into glycerine and fatty acid, due to the activity of the fat-splitting ferment *steapsin.* Such a fat as stearin, under the hydrolytic influence of the ferment, takes up three molecules of water, and splits into three molecules of stearic acid and one of glycerine: and the fatty acid thus set free combines with the alkali of the pancreatic secretion and of the bile to form soap. The acidity of the intestinal contents is largely due to this constant liberation of the fatty acids by steapsin, together with a similar action by the fat-splitting bacteria of the canal, and the formation of lactic acid by the action of micro-organisms on the carbohydrates of the food already referred to.

The **intestinal juice (succus entericus).**—The term *succus entericus* is applied to the secretion of the mucous membrane of the small intestine derived from Lieberkühn's follicles. It may be obtained by either Thiry's or Vella's method, both of which consist in the separation of a portion of the gut from the rest and its fistulous connection with the exterior of the body. In both methods the upper and lower ends of the remainder of the intestine are sutured together so as to restore the continuity of the shortened canal. In Thiry's method the isolated piece of gut is closed at one end by sutures, the other end being stitched to the

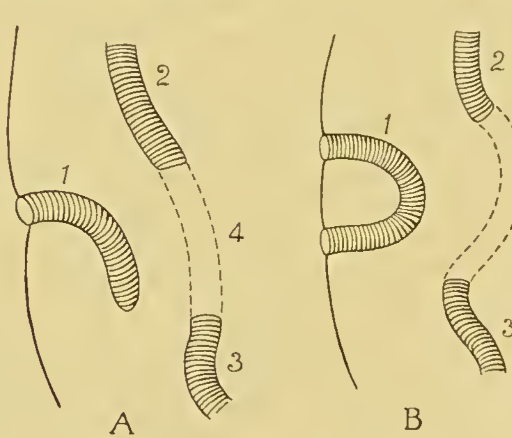

Fig. 251. Fig. 252.

SCHEME OF INTESTINAL FISTULA.

A. Thiry's, and B, Vella's fistula; 1 loop of gut, separated, but with attached mesentery; 2 and 3, upper and lower ends of rest of gut, which are stitched together; 4, dotted line representing separated portion of gut when *in situ.*

abdominal opening, a sac ending blindly internally being thus formed. In Vella's modification both ends of the isolated portion are sutured to openings in the abdominal wall. In either case, though the portion of the intestine thus treated is separated from the rest of the alimentary canal, so that no food can enter it, its nervous and vascular relations are retained through its mesenteric attachment.

The succus entericus is a clear, watery-looking fluid with a slightly alkaline reaction, containing certain ferments and a considerable amount of mucus; of these ferments, one has been known for long, namely invertin—an enzyme acting on maltose and converting it into dextrose.

The other ferments have only recently been made out, indeed little can be said with any degree of certainty of their nature or function; one acts on the simpler forms of proteid, as albumoses and peptones, and is called erepsin, splitting them up into very simple types, such as the amido-acids, &c. Whether this ferment is called into play in the processes of ordinary digestion is more than doubtful, though it is probable that it plays a part in the formation of some of the constituents of the fæces. A second ferment present in the juice is enterokinase or zymolysin; it is supposed that this agent acts upon the zymogens, transforming them into the active ferments: thus while an absolutely fresh and pure sample of the pancreatic juice is practically inert, it becomes intensely active if a little intestinal juice be added to it. Whilst it is probable that this enterokinase acts more or less on all the zymogens, the action is by far the most marked in the case of trypsinogen.

Brunner's glands in the duodenum appear to be continuations of the glands of the pyloric end of the stomach, and are said to produce a ferment which converts proteid to peptone in an acid medium.

The pancreatic, unlike the gastric juice is not antiseptic, and *bacteria* consequently play a distinct part in the changes which the food undergoes in the intestine. The action of the bacteria resembles that of the natural ferments of the pancreatic juice, and through it starch and proteids are converted to sugar and peptones, and the latter to leucin and tyrosin. They can also split up fats like steapsin. But, in addition, they possess more special actions of their own, such as the lactic acid fermentation of carbohydrates, which they may carry further with the formation of carbonic acid, hydrogen and butyric acid. They also produce indol, skatol and phenol as a further stage in the breaking down of proteid substances.

The biliary secretion of the liver.—We may now turn to the consideration of the bile, which, as we have seen, enters the duodenum by an orifice common to it and the pancreatic juice. The liver is a compound tubular gland, the largest gland in the body, the structure of which will be described in detail later, when its glycogenic function is considered. The bile secreted by the liver cells, and collected by numerous interlobular ducts from the gland tubules, passes by the hepatic duct into the cystic duct to the gall bladder, in which it accumulates, and from which it is thrown periodically into the intestine through the common bile duct. Bile is a yellowish, golden-brown, or greenish fluid, with a neutral or faintly alkaline reaction and a specific gravity which varies according to whether it is taken from the gall bladder or obtained by means of a biliary fistula from the hepatic duct; in the former case in man being from 1026 to 1036, and in the latter about 1019. This variation in the specific gravity is accompanied with a corresponding difference in the proportion of solids, bile from the bladder containing from 9 to 14 per cent., while fistula bile contains 1·5 to 3 per cent. Bladder bile, moreover, contains a large quantity of mucus, that taken from the hepatic duct little or none.

The quantity of bile secreted in the twenty-four hours is estimated at from $\frac{3}{4}$ to 1 litre. The secretion is constant, though it only passes into the duodenum at intervals, and there thus fall to be distinguished from each other the *bile-secreting* and the *bile-expelling* mechanisms. The bile-expelling mechanism, represented by the muscular fibres of the gall bladder and larger bile ducts, is thrown into action when the acid chyme flows over the biliary orifice in the duodenum, and except at such times no bile is normally discharged into the intestine. The secretion of bile, on the other hand, is continuous, and rises and falls much as that of the pancreas does. Thus it rises quickly after a meal to a maximum between the fourth and eighth hours, and this is succeeded by a fall, followed by a second rise (a smaller one at the fourteenth or fifteenth hour), after which it again gradually declines. As in the case of the pancreas, the first rise may be due to reflex action and the second to the influence of the absorbed products of digestion on the hepatic cells.

Of the nervous influences acting upon the liver little is known. The gland receives its supply from the splanchnics and vagi through the solar plexus, the constrictor fibres for the hepatic artery being contained in the splanchnics and the dilator fibres in the vagi. But the vascular supply of the liver is to a large extent independent of direct nervous influence, as the amount of

blood passing through it depends not on the hepatic artery, but on the dilatation or constriction of the venæ portæ, and this is influenced by the state of activity or rest of the alimentary canal; the venæ portæ being dilated when food is being digested and constricted when digestion is not taking place. Though secretion is not, as we have seen in the case of the salivary glands, necessarily the consequent of dilatation of the blood-vessels supplying the gland cells, it is nevertheless found that stimulation of the medulla, of the spinal cord, or of the splanchnic nerves, by causing constriction of the abdominal vessels generally, checks the flow of blood to the liver and at the same time checks the flow of bile, and probably the reverse of this takes place in digestion—the increased flow of blood to the liver, brought about by dilatation of the blood-vessels of the alimentary organs generally, laden as this blood is with the products of digestion, may be sufficient to account for the second rise in the amount of the biliary secretion.

Bile, unlike pancreatic juice and like saliva, is secreted at a higher pressure than that in the blood-vessels supplying the gland, or, to be more accurate, at a higher pressure than that of the mesenteric and portal veins, but at a lower pressure than that of the arteries of the body generally. When the escape of bile from the gall bladder is hindered by obstruction of the common bile duct, reabsorption of the biliary constituents from the interlobular ducts of the liver takes place into the lymphatics surrounding them, leading to the condition known as jaundice.

Composition of bile.—The following is the composition of bile, in the one case taken from the gall bladder and in the other from a biliary fistula—

Normal (Bladder) Bile.	Biliary Constituents.	Fistula Bile.
9·14	Bile Salts.	0·6280
1·18	Cholesterin, lecithin, fat.	0·0990
2·98	Mucus.	0·1725
	Pigment.	0·0725
0·78	Inorganic Salts.	0·4510
14·08	Total Solids.	1·4230
85·92	Water.	98·5770
100·00		100·00

The higher percentage of solids in the one is seen to be due to the greater quantity of bile salts it contains, and the comparative scarcity of them in the other is to be accounted for by the fact that normally the salts are split up in the intestine in the process of digestion and a considerable part of them reabsorbed, to again take part in the production of fresh secretion. Now, in the case of a biliary fistula, as the bile is conducted outside the body, and of course never reaches the intestine, this "bile circulation" does not take place, and material required for the continued supply of bile salts in normal quantity is lacking.

As the foregoing table shows, in neither fistula nor bladder bile are there any proteids, nor in man are there any ferments present. The *mucus* which is found in bladder bile is derived from the goblet cells and mucous glands of the larger bile ducts and gall bladder.

The *inorganic salts* are mostly those of sodium, *e.g.*, sodium chloride and phosphate, and the earthy phosphates. Of *iron*, in the form of phosphate, small traces are present, and this iron is derived from the hæmoglobin of the coloured corpuscles, which undergoes changes in the liver, resulting in the formation of the bile pigment. The fats are represented in the bile by *lecithin*. *Cholesterin*, which, as we have seen, is not, properly speaking, a fat, but an alcohol, is always present, and sometimes in considerable quantity, when it may form the greater part of the concretion called gall stones. The form of its crystals has already been alluded to (page 20). Some of its chemical reactions are rather striking. With concentrated sulphuric acid the crystals turn violet or red, and on the addition of iodine a play of colours is seen, ranging from red through blue and green to violet. Again, a solution of cholesterin in chloroform yields a blood-red colouration on the addition of concentrated sulphuric acid, turning to blue, green and yellow, the acid beneath the solution exhibiting a green fluorescence. The physiological significance of cholesterin is not at present known.

The pigments of the bile.—These are *bilirubin* and *biliverdin*, the latter being an oxidation product—the first in a series—of the former. The golden-red colour of human bile is due to the predominance in it of bilirubin, the green colour of the bile of herbivorous animals to the predominance of biliverdin. Bilirubin has the formula $C_{16}H_{18}N_2O_3$, forms a great part of gall stones, and occurs in the urine of jaundice. Its solubilities, which differ markedly from those of biliverdin, are mentioned on page 13. It is readily converted to biliverdin ($C_{16}H_{18}N_2O_4$) by oxidising agents, and the conversion of the latter to bilicyanin,

bilipurpurin, and finally to choletelin are but further stages in the same process of oxidation. Gmelin's test for bile pigments (the addition to the solution of impure nitric acid) is founded upon these successive oxidations, which afford a play of colours passing from red or green through blue-violet and red to yellow. But mere exposure to air of an alkaline solution of bilirubin will convert it to biliverdin, and apparently admixture with the gastric juice as in biliary vomiting will produce the same result.

Neither of the bile pigments show any absorption bands with the spectroscope, though, as we shall see, they are derived from the pigment of the blood. Bilirubin crystallises in the form of rhombic plates or prisms. Biliverdin has not yet been obtained in crystalline form.

If a solution of bilirubin in dilute caustic soda be treated with sodium amalgam a pigment is formed as a reduction product, which is called *hydrobilirubin* and has the formula $C_{32}H_{40}N_4O_7$. The acid solution of this substance shows an absorption band between b and F. Hydrobilirubin is probably identical with the urinary pigment *urobilin*, the form in which *stercobilin*, the pigment of the fæces (which is derived from bile pigment by reduction processes taking place in the intestine), is excreted in the urine after reabsorption. Now, not only can hydrobilirubin (urobilin) be prepared by the reduction of bilirubin as described, but also by the reduction of hæmatin, and we have here, therefore, an indication of a close relationship between the blood and bile pigments: for if urobilin can be produced by the reduction of either, it argues an important relation of the substances themselves to each other. And indeed the evidences that the bile pigments are derived from the hæmoglobin of the blood are conclusive and now generally accepted. These evidences may be stated shortly as follows :—

In the first place, in old extravasations of blood into the tissues the hæmoglobin undergoes changes leading to the formation of hæmatoidin, an iron-free substance, practically identical with bilirubin. Again, if hæmoglobin be split up into its proteid constituents, globin and hæmatin, the latter when deprived of its iron yields hæmatoporphyrin, which is almost identical in its formula with bilirubin. Thirdly, as we have just seen, urobilin can be prepared by the same means from both hæmatin and bilirubin.

From these chemical relations of bilirubin we may pass to the experimental evidence of its connection with the hæmoglobin of the blood. If free hæmoglobin (*i.e.*, hæmoglobin separated from the corpuscles which normally contain it) be injected into the

blood-stream the pigment of the bile is increased in quantity and bile pigment appears in the urine. It appears that the hepatic cells have the power of splitting up the hæmoglobin, first probably into the proteid globin and hæmatin, and then separating the iron from the latter with the formation of bilirubin. Some of the iron is retained in the liver cells and some appears in the bile in the form of phosphate.

That the splitting up of the free hæmoglobin in the blood takes place in the liver and not in the blood-vessels of the body generally (*i.e.*, not in the blood itself) is shown by the fact that if the liver in birds be excluded from the problem by ligature of the portal vein and hepatic artery, no bile pigment appears in the blood or urine; whereas if the liver merely *separated* the already formed pigment from the blood it necessarily would accumulate under these conditions. If the vessels of the liver are not interfered with, but the bile duct ligatured instead, bile pigment soon appears in the blood.

That the pigment appears in the urine as well as in increased quantity in the bile after the intravascular injection of a solution of hæmoglobin cannot be regarded, in face of the above important argument, as an indication that it may be normally formed in the blood itself, for it is readily explainable in other ways. Thus the liver cells can discharge the products of their activity into the blood or lymph as well as into the bile ducts, and under certain conditions may do so when they do not normally. Against the view that the bile pigments may be formed apart from the liver normally, it may also be mentioned that when the liver is withdrawn from the circulation in the manner already described, and a solution of hæmoglobin injected, no bilirubin appears in the blood.

Normally the free hæmoglobin is passed into the blood of the portal vein from the spleen, in the cells of which organ red blood-corpuscles are known to undergo disintegration; and though bilirubin is still secreted with the rest of the bile after removal of the organ, this merely shows that the red blood-corpuscles probably undergo disintegration in other parts of the body, though no doubt to a less extent. It seems probable that the hæmolymph glands may be concerned in this destruction, but the matter cannot be regarded as decided.

The bile salts.—These consist of *glycocholate* and *taurocholate of soda*, the proportion of the two differing in different animals. Thus in man the former is the most abundant, and this also holds good for the herbivora; in carnivora, on the other hand, taurocholate of soda predominates or may alone be present. If

either of these bile acids be boiled with dilute acid or alkali it takes up water and splits into *cholalic acid* and a nitrogenous product, which in the one case is termed *glycin* and in the other *taurin*, thus:—

$$\underset{\text{(Glycocholic Acid)}}{C_{26}H_{43}NO_6} + H_2O = \underset{\text{(Glycin)}}{C_2H_5NO_2} + \underset{\text{(Cholalic Acid)}}{C_{24}H_{40}O_5}$$

$$\underset{\text{(Taurocholic Acid)}}{C_{26}H_{45}NSO_7} + H_2O = \underset{\text{(Taurin)}}{C_2H_7NSO_3} + \underset{\text{(Cholalic Acid)}}{C_{24}H_{40}O_5}$$

Glycin is amido-acetic acid, and taurin amido-isethionic acid. Taurin contains sulphur, while glycin has none. Taurin is found in many tissues, and glycin is doubtless a product of tissue metabolism, the cholalic acid being produced by the hepatic cells, in which its combination with taurin and glycin probably takes place. In the intestine these latter are again separated from the cholalic acid and undergo reabsorption, no doubt to again take part in the formation of bile salts; and it is from the loss of these substances, as already stated, that fistula bile yields so small a. percentage of solids.

Pettenkoffer's test for bile acids consists in the addition of concentrated sulphuric acid to a mixture of the solution with cane-sugar, when a brilliant purple colour results if these are present, due to the interaction of cholalic acid with furfurol, produced by the action of the sulphuric acid on the sugar.

The uses of the bile in digestion.—Bile is chiefly an excrement, but it possesses the property of assisting the pancreatic juice in the emulsification of fats, though by itself it possesses no such power, or only to a very slight extent. No very satisfactory explanation of its power to assist the pancreas is at present forthcoming. It has some power of dissolving fats, and with fatty acids it forms soaps which are soluble in bile and in solutions of bile acids, and this power of dissolving soaps which themselves favour emulsion has been suggested as the explanation of the aid it renders the pancreatic juice in the emulsification of fats.

The bile contains no proteolytic, sugar-forming, or fat-splitting ferments.

It precipitates acid-albumin, albumose, and pepsin from a digestive mixture, the precipitate being soluble in excess, but the pepsin is rendered inert towards proteids. Part of the bile salts themselves is precipitated too in the early part of the experiment. Bile salts reduce the surface tension of water, and for this reason ox gall is used by water-colour painters; and it is held by many that in a similar way bile favours the passage of fat through the intestinal epithelium; for oil will pass through a filter paper wetted

with a solution of bile salts when it will not do so through one wetted with water only. To some extent bile is antiseptic.

Effect of the intestinal juices on the chyme.—When the acid chyme leaves the stomach and enters the duodenum, it encounters the outpouring of the bile and pancreatic juice, the first result of which is that the acid-albumin, albumose and pepsin are precipitated and form a granular coating on the surface of the duodenal mucous membrane, the pepsin being at the same time rendered inert. As the bile and pancreatic juice continue to enter the intestine, the acidity of the chyme is further reduced, and the reaction in this part of the gut may temporarily become alkaline. The trypsin of the pancreatic secretion now destroys the inert pepsin of the gastric juice and commences to act upon the various proteids of the chyme, converting those not already peptonised to peptones: but we do not know to what extent the action is carried further; we do not know in fact to what extent laboratory experiments in this respect represent what actually takes place in the intestine itself, for in many important ways the conditions are different. Some at least of the peptone may be split up into leucin and tyrosin, as these have been found in the intestinal contents, but we cannot say to what extent this normally occurs.

The conversion of starch to sugar, interrupted by admixture of the gastric juice with the food in the stomach, is resumed by the amylolytic ferment of the pancreatic juice with greater vigour.

The pancreatic juice emulsifies fats, and also splits them into glycerin and fatty acids, the latter of which combine with the alkali of the intestinal secretions generally to form soaps. These latter, however, are not absorbed as such, and their object seems mainly to promote emulsification of neutral fats, preparatory to their passage through the epithelium into the lacteals; the bile, as has been suggested, promoting the solution of the soaps as they are formed.

The succus entericus has little or no power of emulsifying fats. It may assist in the peptonising of proteids, and it has the power of inverting cane-sugar.

In addition to the ferments of the pancreatic juice, the bacteria in the intestine exhibit their special action upon the foodstuffs in their passage through the canal, producing lactic and butyric acids from sugar, and leucin, indol, skatol, &c., from proteids. As the chyme mixed with pancreatic juice and bile passes down the intestine, the peptones, sugar and fats are constantly absorbed by the mucous membrane, and pass, as we shall see, either into the

blood of the portal vein or into the lacteal system. The balance of water, however, remains the same, the contents of the intestine maintaining about the same fluidity throughout its extent.

In the **large intestine** the reaction of the intestinal contents becomes distinctly acid, even if it were not so before, owing, however, to the acid fermentation of carbohydrates already mentioned, for the reaction of the secretion of Lieberkühn's follicles is alkaline. Bacteria are especially active in this portion of the canal, and can even break up cellulose with the formation of carbon dioxide and marsh gas. The most striking change, however, that takes place in this part of the gut is due to the absorption of water from the contents, whereby the fluid chyme becomes changed to the more solid fæces, to the formation of which the mucous cells of Lieberkühn's glands contribute their secretion.

The *fæces* consist of the undigested portions of the food, such as cellulose, elastin, and horny epidermis, and sometimes even starch grains when these have not been boiled. The colour is due to the presence of stercobilin, which is derived from the bilirubin of the bile by reduction in the intestine, and which seems identical with the urobilin of the urine. The ordinary biliary pigments are absent, but amongst the products of the decomposition of the bile acids a little taurin and cholalic acid are found: the glycin, most of the taurin, and a great part of the cholalic acid having been reabsorbed. Skatol, indol and other substances formed by the bacterial decomposition of proteids give to the fæces their peculiar odour, skatol being the chief of these. The fæcal odour of the intestinal contents commences in the lower part of the ileum.

Other substances which are found in the fæces are albumin, cholesterin, fatty acids, insoluble soaps of magnesia and calcium, phosphates, especially triple ammonio-magnesic phosphate, other inorganic salts, mucin, &c.

The contents of the intestine in new-born infants is termed *meconium* and consists of concentrated bile, the pigment being a mixture of bilirubin and biliverdin.

Movements of the intestinal wall—peristalsis.—Two kinds of movements occur in the intestine—(1) Gentle swaying pendulum movements, often recurring rhythmically at the rate (in the dog) of 10 or 12 a minute: both muscular coats are involved in the movement, which, starting at any part of the gut, travels from above downwards at the rate of 2 to 5 centimetres per second; and (2) true peristaltic movements, in which a ring of constriction passes slowly down the gut at the rate perhaps of 1 millimetre

per second. At the site of the ring the lumen of the tube is practically obliterated, while the portion of intestine immediately below is relaxed, a wave of inhibition thus preceding the wave of contraction. These peristaltic movements under normal conditions travel downwards and end at the ileo-cæcal valve. They are most readily initiated by mechanical stimulation of the mucous membrane, *e.g.*, with a bolus of food.

The first movement, which we have described as a swaying one, is apparently *myogenic*, that is the slight waves of constriction are due to an inherent quality in the muscle-fibres themselves, and pass along the intestinal wall from one fibre to another. They do not move the food onwards, and they seem chiefly of use in mixing the intestinal contents. On the other hand, the peristaltic movement is excited by the stimulation caused locally by a bolus of food or experimentally by a bolus of cotton wool and vaseline introduced into the gut, and the result of such stimulation is immediate and marked. It consists of a two-fold effect as already stated, *i.e.*, of excitation above the point of stimulation and inhibition below it. The ring of constriction travels slowly down the intestine, driving the bolus before it. But these results of stimulation are at once put an end to by painting with cocaine or injection of nicotine. The rhythmic swaying movements, on the other hand, continue as before, though they cannot, as we have seen, drive the bolus along the gut. The explanation of these things appears to be that the peristaltic movements are directed by Auerbach's plexus, that they are indeed of the nature of co-ordinated reflexes carried out by a local nervous mechanism. The movements of the large intestine resemble those of the small, and extend from the ileo-cæcal valve downwards to the rectum, which is not, however, involved in the action except during defæcation.

Nervous relations of the intestine.—The intestine is not so dependent as the œsophagus on the nervous system for its peristaltic action, for typical movements may be induced by local stimulation, as by the presence of food, when all the nervous connections have been severed. Again, peristalsis is stopped by an interruption to the continuity of the muscle, though all the nerves remain intact.

But though the intestine can thus be considered capable of independent action, it is no doubt under normal conditions largely influenced by the nervous system, for peristalsis may be augmented or inhibited by stimulation of the nerves supplying it; and probably augmentory impulses form part of a normal

reflex act through the medulla, starting in the intestinal wall itself. The small intestine is supplied by branches of the right posterior vagus and the splanchnics, which reach it through the solar plexus.

Stimulation of the vagus induces contractions of the intestinal wall, accompanied with vascular dilatation, while stimulation of the splanchnics inhibits the movements, and causes constriction of the vessels. The splanchnic fibres would appear to be constantly in action for the intestinal movements are strengthened by their section. Reflex inhibition of the movements through the splanchnics may be caused by any painful excitation of a sensory nerve, especially in the abdomen. It is possible that intestinal movements, such as peristalsis, though, as we have seen, induced by the direct stimulus of contact with food acting on a strictly local mechanism, may also be encouraged by a further reflex action through the medulla, the branches of the vagus being the efferent fibres. As we have already had occasion to mention, swallowing or even the smell of food has been observed to increase the contractions of a loop of intestine separated from the rest, but with its nervous connections still retained.

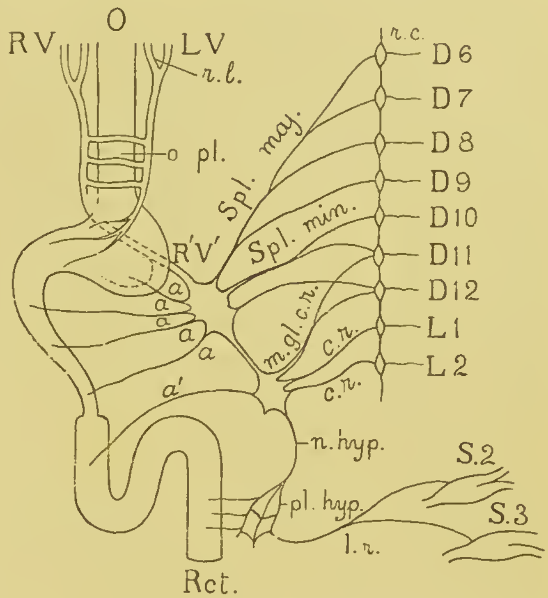

Fig. 253.—Diagram of Nerves of Alimentary Canal.

O, Œsophagus; *Rct.*, rectum; *LV*, left vagus passing in front of stomach; *r.l.*, recurrent laryngeal; *RV*, right vagus, passing behind stomach and continued as *R V'* to join solar plexus; *o.pl.*, œsophageal plexus; *a*, branches from solar plexus to stomach and small intestine; *a'*, branches from inferior mesenteric ganglion to large intestine; *Spl. maj.*, great splanchnic nerve; *Spl. min.*, small splanchnic nerve; *m.gl.*, inferior mesenteric ganglion; *n.hyp.*, hypogastric nerve; *pl. hyp.*, hypogastric plexus; *r.c.*, rami communicantes; *c.r.*, nerves from the ganglion, &c., belonging to eleventh and twelfth dorsal and first and second lumbar nerves; *l.r.*, nerves from the second and third sacral nerves, *S2*, *S3*.

Want of oxygenation of the blood in the intestinal wall is a potent stimulus for peristalsis, as may be seen when the abdomen of an animal is opened immediately after death, when an exaggerated picture of the normal contractions is presented.

Of the drugs affecting peristaltic action, some act locally on the bowel, others on the central nervous system. Thus muscarine is a local stimulant, strychnine a central one, while morphia acts locally as a depressant.

The nervous supply of the large intestine, or at least of its lower part, and of the rectum is derived in the dog from the second and third sacral nerves, and from the anterior roots of the two last dorsal and first two lumbar nerves. The dorsal and lumbar branches pass through the inferior mesenteric ganglion and join the hypogastric plexus, from which they pass with the sacral branches to the intestinal wall (Fig. 253). The sacral nerves correspond to the vagus in their action, and when stimulated cause contraction of the descending colon and rectum, while stimulation of the dorsal and lumbar branches leads, like that of the splanchnics higher up, to inhibition of the peristalsis. Both coats of the intestine are affected in the same manner at the same time.

This part of the intestinal canal is much more dependent for its muscular activity on the central nervous system than the rest. The reflex centre lies not in the medulla but in the lumbar part of the cord, and is very intimately concerned with the movements of the descending colon and rectum, which are almost entirely, if not quite, governed by it; and not, as is the case in the rest of the gut, due to an inherent quality of the muscular fibres themselves or the action of a local reflex mechanism in the wall of the canal itself. Clinically this is of interest, as it accounts for the prevalence of constipation in diseases of the central nervous system.

Defæcation.—It is especially in the expulsion of the fæces from the lower end of the large intestine that this reflex mechanism is involved. As the solid fæces accumulate in the large intestine, especially in its lower part, they give rise reflexly to increased peristaltic action, which leads to their propulsion through the sigmoid flexure into the rectum, where a similar peristalsis is set up. As the fæces enter this part of the canal, and proceed towards the anus, they give rise to two further kinds of nerve action—(1) A purely reflex one, the part of the lumbar centre which presides over the sphincter ani, and usually maintains it in a state of tonic contraction, being inhibited by afferent impulses from the mucosa of the rectum, and the sphincter relaxed in consequence; and (2) a sensory one, the impulse being conveyed to the brain from the same surface, and giving rise to a desire to evacuate the bowel. This sensory impulse may have

either of two results—(*a*) If the fulfilment of the desire is to be temporarily postponed, impulses are transmitted from the brain to the lumbar centre, which tend to restore its tonic action on the sphincter, in other words, to nullify the inhibitory effect on the local centre of the afferent impulses reaching it from the rectal mucosa ; and, in addition, the external sphincter of the anus, consisting of striped muscle, may be thrown into contraction by an ordinary motor impulse, to take its part in preventing the escape of fæces at the anus ; (*b*) if the desire is to be immediately carried out, impulses are sent from the brain, putting into action the voluntary portion of the mechanism of defæcation. This consists in an impulse to the lumbar centre from the brain still further increasing the reflex effect of the stimulation of the rectal mucosa ; and the taking of a deep inspiration, followed by closure of the glottis and contraction of the abdominal muscles, whereby the contents of the descending colon are pressed onwards into the rectum, from which they are completely expelled by the peristaltic contraction of the thick muscular walls.

Thus, under ordinary circumstances, defæcation is partly a voluntary and partly a purely reflex act, but it is to be noted in this connection, that when the lumbar centre has been entirely separated from the brain by division of the cord above the lumbar region, defæcation in dogs may be completely carried out, and in this case the action must be purely reflex. The same purely reflex action may take place in human beings where voluntary control has become lost through disease.

The position of the lumbar centre has been defined by the fact that section of the cord above its level does not (after the temporary effect of the operation has passed off) abolish its activity ; and if the nervous strands between the rectum and the cord be interrupted, the sphincter becomes relaxed.

When the abdominal walls contract, and so exercise pressure on the floor of the pelvis, the levatores ani are thrown into action at the same time to give support to the parts and to prevent protrusion of the rectum.

CHAPTER X.

THE LYMPHATIC SYSTEM—THE SPLEEN, THYMUS, &c.

WE have now considered the changes the food undergoes in its passage through the different parts of the alimentary canal, and in the next chapter we shall pass to the consideration of the mechanism of "absorption," whereby the various food substances pass through the epithelial lining and the rest of the alimentary wall outside it to their subsequent destination. We shall find that towards this goal—the tissues—two main paths lie open, of which one is by the radicles of the portal vein to the liver and so to the inferior vena cava—the directly vascular path; while the other is by the lymphatic radicles of the villi of the small intestine and the mesenteric lymphatic vessels to the receptaculum chyli and the thoracic duct to the veins at the root of the neck. Of these two paths we shall see that while the proteids and carbohydrates select the first and thus pass directly into the blood-stream, the fat enters the lymphatic radicles and is carried to the thoracic duct, thus entering the blood-stream through the medium of non-vascular channels.

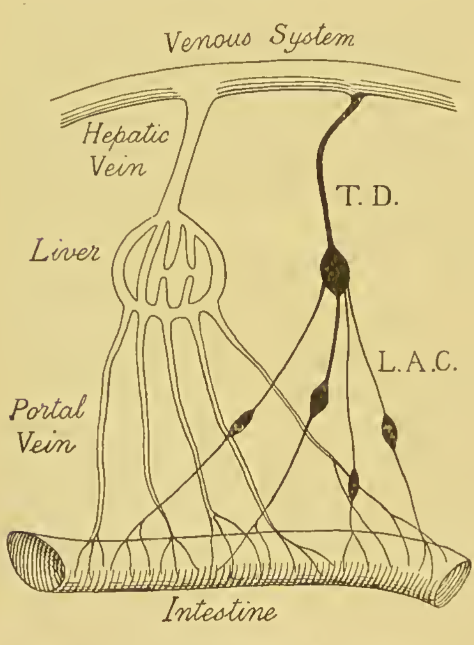

Fig. 254.—Scheme of Intestinal Absorption.

L.A.C., Lacteal; T.D., thoracic duct.

By the blood the food substances are conveyed to all the tissues, in which they undergo important changes, each tissue reacting

upon them to its own advantage; and these changes will be considered under the heading "Metabolism." We know a little of the prominent superficial features of the metabolic changes, but the complete inner story of the complex processes, whereby living protoplasm takes up dead matter which then puts on the attributes of life itself, will perhaps be forever hidden from us. On the other hand, the study of the final products of metabolism excreted from the body, like that of the food taken in, presents little difficulty, these final products being, generally speaking, urea, carbonic acid and water, which are cast off by one or other of the lungs, kidneys, and skin. This phase of the history of food will be considered under "Excretion."

In the present chapter, however, neither Absorption, Metabolism, nor Excretion can be dealt with; but we must turn aside for a moment to study the characters of the lymphatic system generally, of which the radicles in the villi of the intestine, the mesenteric vessels and glands and the lymphatic duct form so important and striking a part. It will be convenient, too, to include in this chapter the description of some of the "blood-glands," such as the spleen and thymus.

The Lymphatic System.

The tissues of the body generally are saturated with a fluid termed *lymph*, which resembles the plasma of the blood except that the proportion of solids present is much less. The lymph from the intestine during digestion contains, in addition, fat, and is known as *chyle*, which finds its way through the mesenteric lymph-channels into the receptaculum chyli of the left thoracic duct; and the latter after receiving lymph from other parts of the body opens into the junction of the left subclavian and jugular veins. A small right thoracic duct opens in a corresponding way on its own side. The lymph as a fluid distinct from the blood becomes lost, therefore, when the ducts join the venous trunks, the two being here mixed together and carried to the right side of the heart, thence to the left through the lungs, from which it is returned by the pulmonary veins to the left side of the heart, and thence to the capillaries in the tissues through the aorta and systemic vessels generally. Through the walls of the capillaries lymph passes into the lymph-spaces in the connective tissues in which the capillaries lie. From these spaces it is gathered into larger lymph-capillaries with a definite epithelial wall and these in turn transmit it to the lymphatic vessels, which in their structure resemble veins. From these vessels it is

received into the vertebral trunks, which pour it again into the blood-stream at the root of the neck. Here and there throughout the body lymph-glands are to be found on the course of the lymphatic vessels. We may now examine some of these parts more closely.

The origin of the lymphatics.—The lymphatic channels in the tissues may be considered to commence in the **lymph-spaces,** of which by far the largest number are represented by the spaces occupied by the cells. In areolar tissue the areolæ between the interlacing bundles of fibres form an additional series of larger spaces, the cells clasping the bundles exhibiting a tendency to form an imperfect lining for their walls. From these spaces, which we have seen form an intercommunicating network in the case of the cell spaces proper, through the medium of the anastomosing channels in which the processes of the contained cells lie, the lymph passes into the **lymph-capillaries**—tubular anastomosing passages of considerable breadth lined by a single layer of nucleated squamous cells with a sinuous outline. In a specimen of flattened tendon, such as that of the diaphragm, stained with nitrate of silver, it will be seen that the clear unstained cell spaces in immediate proximity to the margin of the capillary labyrinth, also unstained, communicate with it through the anastomosing channels or canaliculi proceeding from them, and one of these capillaries may frequently be seen to disappear terminally by breaking up into a number of cell spaces. According to this view of the connection of the cell spaces and the capillary, the sinuous cells lining the latter would be regarded as differentiated connective tissue corpuscles, and the labyrinth itself as composed of a series of differentiated connective tissue lymph-spaces of the larger kind.

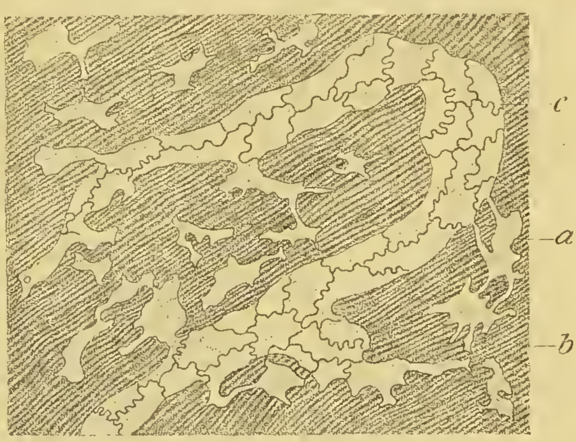

Fig. 255.—Central Tendon of Diaphragm of Guinea-Pig.

a, Cell space; *b*, intercellular matrix; *c*, lymph-capillary.

Speaking generally, every tissue is permeated with lymph through an anastomosing system of lymph-spaces; and the

importance of such permeation is well seen in the case of tissues such as bone cartilage and the cornea, which are virtually extra-vascular and which depend for their nutrition entirely upon the stream of lymph flowing through their cell spaces, which form with their canaliculi an anastomosing system of channels. These channels are not so obvious in hyaline cartilage it is true, but from the analogy of the cartilage of the squid, in which the cell spaces communicate with each other by well-marked canaliculi, we may infer that some communication of the same kind exists in ordinary mammalian cartilage.

The *central lacteal of a villus* may be regarded as a lymph-capillary, in this case ending blindly, for there is here at all events no anatomical evidence of communication between the lumen of the lacteal and the meshes of the adenoid reticulum in which it lies. The lymph from the capillary network in the villus traverses the adenoid reticulum between it and the lacteal, and with the finely divided fat it bears, passes through the lacteal wall and is carried to the network of lymph-capillaries in the deeper part of the mucosa, with which the central lacteal is continuous. The lymph-capillaries and the central lacteal are here, as elsewhere, lined with a single layer of flattened epithelial cells with a sinuous outline.

Perivascular lymphatics.—Lymph-capillaries are sometimes in certain situations (as in some parts of the central nervous system) placed outside small blood-vessels, that is to say so as to envelop them with a double tubular sheath; the outer layer being at a little distance from the vessel wall while the inner is reflected upon its surface.

The *serous cavities*, such as the pleural, the pericardial and the peritoneal, are of the first importance in the economy of the body and of great interest in their lymphatic relations. They may be regarded as exaggerated lymph-spaces, which have been greatly extended to subserve certain purposes, amongst others the free frictionless movement of the organs they invest upon neighbouring parts.

The tunica vaginalis is another instance of such an extended lymph-space, as are also bursæ and the synovial sheaths of tendons, though these contain a more viscid fluid than ordinary lymph.

If we study such a lymph-sac as the pleura we find it represented by an extended space, so large indeed that it has split the fibrous tissue in which it lies into two sheets—a parietal one applied to the chest wall, and a visceral one covering the lung itself; and this space is lined with a single layer of flattened

squamous nucleated cells, not sinuous but polygonal in outline. The result of this space, thus lined with a layer of cells lubricated with lymph, is that the lung in expanding and contracting glides readily upon the surfaces surrounding it. The space communicates with the lymphatic system through small stomata or openings between the polygonal cells, which lead to lymph-channels in the connective tissue, on the one hand lining the chest wall and on the other investing the lung itself. Thus the sac is in communication with the lymph-stream in the connective tissue sheet on either side of it.

An ordinary *bursa* is in reality a similar lymph-space but of a more simple kind. The skin over a bony tuberosity requires to work smoothly over it and consequently there is developed in the loose tissue between the two a space incompletely lined with cells of an epithelioid type lying upon a thin condensation of the surrounding tissue which forms the wall of the sac; the space itself containing a viscid glairy fluid in the place of ordinary lymph. Here we have a good illustration of possible adaptation of means to an end. The two surfaces of connective tissue between the skin and the bony tuberosity work upon each other, and forthwith the connective tissue cells at the surface become flattened and attempt to form an epithelial lining for the developing bursal sac; and, in addition, a viscid fluid differing from ordinary lymph becomes secreted in view of the special requirements of the case with regard to friction. Here, as before, the cavity of the sac is in communication with the lymph-stream in the connective tissue supporting it.

The **lymphatic vessels and thoracic duct.**—From the capillary labyrinth the lymph passes into the smallest *lymph-vessels.* These are narrower in diameter than the capillaries from which they spring, consist of a lining of fusiform epithelial cells (not distinctly sinuous in outline) resting on a thin connective tissue basis, anastomose freely with each other, and like veins possess valves. The pressure on the proximal (cardiac) side of the valve causes a certain amount of local distension, and this gives to the vessels a beaded appearance. The larger vessels, into which the smaller ones rapidly merge, possess very much the structure of veins, and to that extent need no particular description. Their walls, however, are thinner, and in consequence of this and the pressure on the cardiac side of the valves they exhibit a beaded condition from local dilatations.

The *thoracic duct*, which receives the chyle from the intestine during digestion and the lymph from the body generally, also

resembles a vein in its general structure. It is to be noted, however, that it does not progressively widen towards its cardiac end as a vein does, its lower end, which receives the chyle and which we have seen is therefore called the receptaculum chyli, being its broadest part. In the thoracic duct, as compared with a vein, the muscular predominates over the connective tissue element, and it is thus less elastic, more friable, and more easily torn. Like lymph-vessels generally it possesses numerous valves—reduplications of the lining membrane—directed towards the heart.

We have mentioned that throughout the body *lymph-glands* are frequently found in the course of the lymph-vessels; and the structure of these we shall consider immediately. Before proceeding to do so, however, it will be well to take note of the **solitary follicles**, as they are called, which resemble them in their relations to the lymph-stream but are much more simple in structure. Solitary follicles are found in some of the mucous membranes of the body in the course of the smaller lymphatic vessels. Thus in the small and large intestines they occur scattered as small pin-head bodies, imbedded partly in the mucous and partly in the submucous coat. They are found collected together in *agminated* or *Peyer's patches* in the small intestine, especially in the ileum along the line of its mesenteric attachment. Solitary follicles are numerous in the cæcum and vermiform appendix, but here they lie wholly beneath the mucous coat. Similar follicles are found in the tonsils, the submucosa of the bronchi and bronchioles, &c.

A solitary follicle consists of a mass of adenoid or lymphoid tissue supporting a network of blood-capillaries, the whole being surrounded with a lymph-space or *sinus* in communication with neighbouring lymphatic vessels. The lymph-sinus is lined by a layer of cells with a sinuous outline, and is traversed here and there by strands of connective tissue passing from the adenoid reticulum within to join the connective tissue in which the follicles lie. The larger of these strands contain blood-vessels, and are covered with sinuous epithelial cells reflected from the epithelial lining of the sinus itself.

The lymphoid tissue within the sinus consists of a delicate fibrillar network covered with epithelial cells—the usual adenoid reticulum—the meshes of the network being crowded with lymph-cells. These are for the most part small round cells with a single large nucleus and little perinuclear protoplasm, and are present in such numbers that the adenoid reticulum is completely obscured. Many of the cells exhibit kariokinetic or mitotic changes, showing that multiplication of their number is going on.

Course of lymph-stream through the follicles.—The lymph on leaving the blood-capillaries traverses the adenoid tissue and passes into the lymph-sinus, from which it enters the general lymph-stream by the lymphatic vessels with which the sinus is connected.

The functions of the follicles seem to be the production of lymph-cells, which pass through imperfections in the inner epithelial layer of the sinus into its lumen and thence to the lymphatic vessels; the arrest and it may be the destruction by the lymph-cells of the adenoid tissue of foreign matter in the lymph passing through; and thirdly there is no doubt a more or less complex interchange between the blood and the lymph-stream. Probably, in addition to the stream already mentioned from the blood-capillaries into the sinus, one in the opposite direction from the sinus into the capillaries takes place; but of the exact nature of the interchange we know little.

Lymphatic glands.—A lymph-gland may be regarded as a solitary follicle which has undergone further development, so that it presents a more complicated structure, and is no longer imbedded in a mucous membrane, but exists as an independent organ. But just as a secreting gland, however complicated, retains the essential characteristics of the more simple forms, so in this case the essential features of a lymph-follicle, as already described, are readily recognisable in a lymphatic gland. The lymph-gland, however, is much larger than a solitary follicle, and instead of being imbedded is exposed upon the course of lymphatic vessels. For this reason it possesses a protecting fibrous capsule from which septa are sent into the substance of the gland for the support of the lymphoid tissue and the increase in the extent of the sinus. How this increase is effected will be apparent from the following description of its structure.

A lymph-gland is a somewhat reniform body which is often of the size of a large pea, but may be smaller or larger. At one side is the *hilum*, which is traversed by the afferent and efferent blood-vessels and the efferent lymphatic vessels; the afferent lymphatics entering the gland through the capsule at various points of the periphery. For here, as in the solitary follicle, we have to consider an afferent and efferent system of lymph-vessels, an intermediate sinus lined with sinuous epithelium, and within the sinus a mass of lymph follicular tissue supporting a network of blood-capillaries. The substance of the gland generally may be roughly divided into a central *medullary portion*, which, however, approaches the surface at the hilum, and a peripheral or *cortical*, which lies immediately

beneath the capsule. The latter consists of two layers of connective tissue, between which runs a network of afferent lymphatic

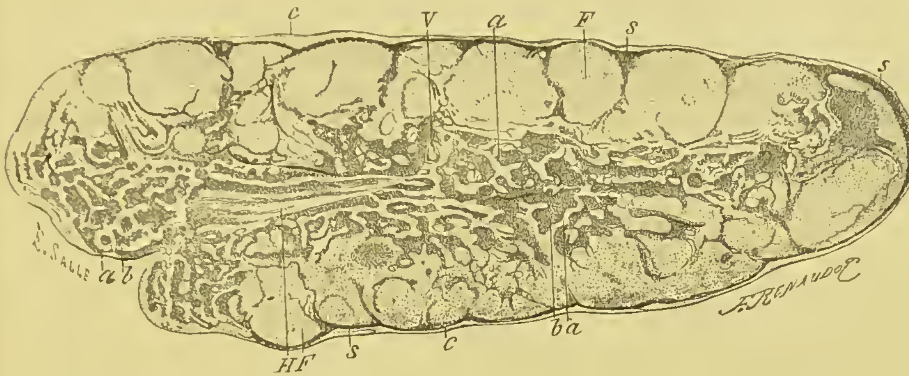

Fig. 256.—Longitudinal Section of Cervical Lymph-Gland of Dog.

c, Capsule; *s*, lymph-sinus; *F*, cortical lymph follicular mass; *a*, medullary lymph follicular cords; *b*, lymph-sinus in the medulla; *V*, section of a blood-vessel; *HF*, connective tissue, blood- and lymph-vessels passing through hilum.

vessels, which open here and there into the lymph-sinus below. From the inner surface of the capsule trabeculæ or septa pass into the gland, dividing the cortex into more or less regular compartments. As the medulla is reached, however, the primary septa undergo subdivision, so that the medullary part of the lymph follicular tissue is more broken up than the cortical. In some animals both the capsule and the trabeculæ or septa contain non-striped muscle-fibres.

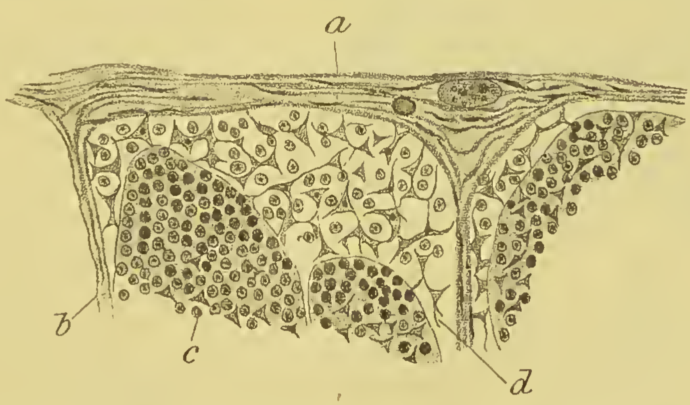

Fig. 257.—Section of Lymphatic Gland (Cortex) (× 60).

a, Capsule; *b*, trabeculæ; *c*, lymph follicular tissue; *d*, sinus traversed with adenoid tissue.

The segments into which the cortex is divided by the septa are of the shape of a truncated pyramid, the broad end of which lies

immediately beneath the capsule, while the narrow end is continuous with the medulla. The central part of one of these cortical segments—indeed the greater part of it—consists of a mass of lymph follicular tissue similar to that of a solitary follicle; while the peripheral part is represented by the *lymph-sinus* which lies between it and the capsule and septa. When these *lymph follicular masses* are traced inwards to the medulla it is found that they become broken up by the septa (which branch and anastomose when this point is reached) into a network of *lymph follicular cords*, and here, as before, the lymph-sinus separates the connective tissue septa from the lymphoid tissue; so that in a lymphatic gland we have a network of connective tissue septa and another of lymphoid tissue, the two being everywhere separated from each other by the intervening lymph-sinus.

The *sinus*, like that of the solitary follicle, is virtually a lymph-capillary, and is lined with a single layer of flattened epithelial cells with a sinuous outline which may be revealed by nitrate of silver. The outer layer of epithelium is applied to the connective tissue framework of the gland, *i.e.*, the capsule and trabeculæ; while the inner layer covers the lymph follicular masses in the cortex and the lymph follicular cords in the medulla. Bridging across the sinus are found here and there bridles of connective tissue containing blood-vessels in passage between the lymphoid tissue and the trabeculæ, and these bridles, as in the case of the similar ones across the sinus of the lymph-follicle, are covered by a reflection of the sinuous epithelium. But in addition to this — and here the lymph-gland is peculiar — the sinus is traversed by an adenoid network — *i.e.*, a fine fibrillar network covered by epithelial cells—the fibrils being continuous with those of a similar network in the lymphoid tissue on the one hand and with the fibrils of the connective tissue trabeculæ on the other; while

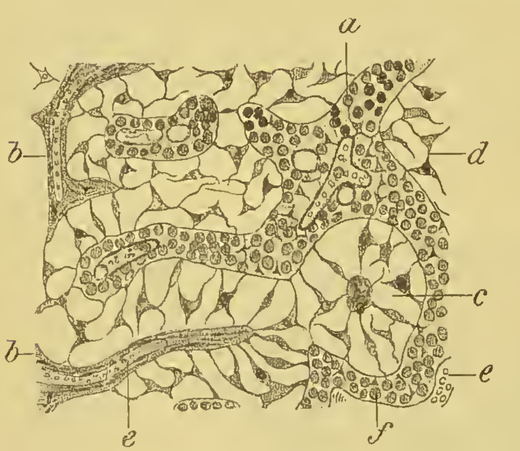

Fig. 258.—SECTION OF LYMPHATIC GLAND (MEDULLARY REGION).

a, Lymph follicular tissue; *b*, trabeculæ; *c*, sinus; *d*, adenoid reticulum of sinus; *e*, blood-vessels in lymph follicular tissue and trabeculæ; *f*, lymph-cells.

the epithelial cells are a reflection of the epithelium lining the sinus. But this network differs from that found in lymphoid tissue generally in being much coarser and stronger, and in the fact that the lymph-corpuscles in its meshes are comparatively few in number; so much so that on pencilling a section with a camel-hair brush, or shaking it in water, a sufficient number of them may be removed to leave the adenoid reticulum plainly visible. And so easy is it of demonstration in this way that the sinus of a lymph-gland is selected, as a rule, to show the nature of adenoid tissue generally.

The *follicular tissue*, both of the cortex and medulla, presents no special structural features to distinguish it from that found elsewhere. It consists of a delicate adenoid reticulum, similar to that of the solitary follicles, the meshes of which are crowded with similar leucocytes or small round lymph-cells. Many of the cells show mitotic changes, and this is often well marked in the cortical pyramidal masses, which in prepared specimens often exhibit a lightly stained centre and more deeply stained periphery. Such a centre is sometimes termed a "lymph-knot," and the lightness of the staining is due to the fact that here the cells are commencing to divide, with the result that their perinuclear protoplasm, which stains less deeply than the nucleus, is increased in quantity. The cells, in short, are larger and less deeply stained, except so far as the chromatin of the nucleus is concerned, and hence that part of the follicular tissue in which these changes are taking place appears lighter as a whole. The lymphoid tissue supports a network of capillary blood-vessels.

Course of the lymph-stream through the gland.—The lymph reaching the gland passes through the network of lymph-vessels in the capsule into the sinus immediately beneath it, and thence through the cortex and medulla, being reinforced by the lymph derived from the capillary network in the lymphoid tissue. After traversing the gland in the sinus it leaves the organ at the hilum by efferent lymphatic vessels.

Course of the blood-stream.—The afferent vessel enters the connective tissue framework by the hilum, dividing again and again as the trabeculæ or septa themselves divide. At intervals small branches are given off from the main divisions, which leave the trabeculæ, cross the sinus, and enter the lymphoid tissue, in which they break up into a blood-capillary network. The veins collecting the blood from this network cross the sinus, enter the trabeculæ, and leave the gland at the hilum, pursuing the same path, therefore, as the arteries but in the opposite direction. It is these vessels crossing the sinus with the small amount of connective tissue

necessary for their support that constitute the "bridles" already referred to.

The functions of the lymph-glands are much the same as those of the solitary follicles. They serve as a sieve in which foreign, it may be microbic, matters are arrested; and thus in the case of a dissecting wound the glands on the lymphatic vessels concerned are early affected. They also serve as centres for the production of leucocytes, the lymph leaving the glands containing a greater number than that going to them. And thirdly, as in the case of solitary follicles, there is a continuous interchange between the blood and lymph-stream in the gland.

To recapitulate: The lymph-stream starts with the transudation from the blood-capillaries into the lymph-spaces of the tissue in which the capillaries lie; and here the lymph yields to the tissue elements food, and receives in return from them waste products. From thence it passes into the lymph-capillary labyrinth, and so into the lymphatic vessels. In passing along these latter it becomes subjected to the action of the lymphatic glands placed upon their course, receiving, as we have seen, an addition of lymph-corpuscles from them, which have passed from the lymph follicular tissue into the lymph-sinus. Finally, the lymph reaches the left or right thoracic duct, through which it joins the venous circulation at the root of the neck.

Now, as the blood leaving one organ differs from that coming from another, so the lymph from any particular part of the organism may have distinctive characters of its own; and of this the most striking instance is afforded by the contents of the mesenteric lymph-vessels, or lacteals as they are sometimes called, during the digestion of a meal. Every meal contains more or less fat, unless such be excluded from it by set purpose, and during digestion the fat is absorbed into the central lacteals of the villi of the small intestine and transmitted by the mesenteric lymph-vessels to the thoracic duct. If at this time the abdomen be opened and the contents examined the mesenteric lymph-vessels are to be seen as white lines running from the intestine across the thin transparent mesentery, their whiteness and opacity being due to the milky fluid, or chyle as it is termed, which they now contain. And the chyle when it reaches the thoracic duct renders its contents as a whole milky too. When digestion is not going on—when fat is not so being absorbed—the contents of the mesenteric lymph-vessels do not differ in character from ordinary lymph.

Composition of lymph and chyle.—Lymph is a colourless alkaline fluid with a specific gravity of 1015 to 1030. Coming

directly as it does from the blood in the capillaries, through a thin epithelial membrane, it possesses many of the characters of blood itself; differing mainly in the absence of the red corpuscles and the smaller percentage of solid matter present. Like blood it will coagulate spontaneously, though the resulting clot is less pronounced and less firm. Lymph contains fibrinogen, serum-albumin, and serum-globulin, neutral fats, urea, and sugar in small quantity, and the same salts as blood. The following table shows the composition of human lymph.

Water		95·0
Solids	Fibrin	0·1
	Proteids	4·1
	Fat	trace.
	Extractives	0·3
	Salts	0·5
		100·0

But though the lymph contains no red corpuscles, or only a few stray ones which are not an essential feature of it, leucocytes, on the other hand, are as numerous as in the blood; the smaller cells with a single nucleus and little perinuclear protoplasm here forming the majority. Of the gases of the lymph we have already spoken under "Respiration"; most of the gas obtainable is carbonic acid, of oxygen there is very little. **Chyle** differs from lymph in the large amount of fat it contains, which is very commonly present to the extent of five per cent., though it may vary considerably from time to time. Some of the fat is in the form of small globules, as in milk, but the greater part is still more finely sub-divided, so much so that it has been termed the "molecular basis of the chyle," and is very characteristic of it. The following analysis of the composition of chyle was made from fluid obtained from a fistula of the human thoracic duct (Paton).

Water	953·4		
Inorganic Solids	6·5		
Organic Solids	40·1	Proteids	13·7
		Fats	24·06
		Cholesterin	0·6
		Lecithin	0 36

The quantity of lymph or chyle passing through the thoracic duct in twenty-four hours has been estimated at from three to four kilos, or nearly as much as the whole of the blood of the body; and of

this half may be considered to come from the alimentary canal, and the rest from the body generally. But these figures are necessarily only approximate, not to say conjectural.

The **movements of the lymph.**—Certain factors contribute to the movement onwards of the lymph in the course laid down for it. Of these the most obvious is the presence of valves in the lymph-vessels, which permit of a flow towards the heart but not in the opposite direction; and in this connection it may be mentioned that a valve guards the opening of each thoracic duct into the subclavian vein of its side, and prevents the passage of fluid from the vein into it. Owing to the valves in the lymph-vessels muscular movement by compressing these channels forces their contents in the only direction it can take—*i.e.*, towards the heart. Moreover, the muscular elements of the villi in contracting during digestion force the chyle in the central lacteal past the valve at its outer end into the lymphatics in the deeper part of the mucosa; and the peristaltic contractions of the muscular coat as a whole encourage its progress to the mesenteric lacteals. Secondly, the pressure in the capillary blood-vessels is higher than in the lymph-spaces, and this than that in the thoracic duct. The pressure in the latter is in its turn greater than that in the subclavian vein, and this difference is increased during inspiration, when, as we have seen, the pressure in the veins near the heart falls still lower and becomes even negative. Thirdly, the flow may be promoted by rhythmical contractions of the muscular walls of the lymphatic vessels, though there is no direct evidence to prove it. In some animals, however, such as the frog, "lymph-hearts"—muscular sacs—are found on the course of the lymphatics, which pulsate at the rate of sixty or seventy beats a minute, and thus undoubtedly favour the circulation of the lymph. Fourthly, apart from the slope of pressure between the lymph-spaces and the subclavian vein already referred to, the osmotic or secretory process (to which we shall refer immediately), whereby the lymph passes through the capillary wall, may be regarded as a constantly acting *vis a tergo* in the circulation of the lymph.

The nervous system has not yet been shown to have a special influence on the stream of lymph apart from the influence of vaso-motor changes increasing or decreasing the pressure in the blood-capillaries. The thoracic duct is said to be under the influence of nerves belonging to the sympathetic system, whereby it may be dilated or constricted.

Relation of lymph and blood.—In connection with the flow of lymph from the capillaries it may be mentioned that the current

under certain circumstances sets in the opposite direction—*i.e.*, from the lymph-spaces into the blood. Thus if fluid be injected into the blood-stream so as markedly to increase its quantity, the excess of fluid is rapidly excreted by the kidneys, but at the same time an increased flow of lymph takes place through the capillary walls into the tissues. On the other hand, after a hæmorrhage reducing the quantity of blood in the vessels, lymph passes from the tissues into the blood-capillaries so that the volume of blood in the vessels may return as rapidly as possible to normal.

Theories of lymph formation.—We have now to ask by what processes the lymph passes through the capillary wall into the lymph-spaces beyond. Is this due to purely *physical* causes, such as filtration and osmosis, or is it due to some *vital* activity on the part of the epithelial cells of the capillaries—an activity analogous to that of the cells of an ordinary secreting gland?

The older view, as taught by Carl Ludwig, was that the lymph passed through the capillary wall in obedience to the laws of filtration and diffusion, and that these laws were sufficient to account for its passage; but to this view there are grave objections. Thus though the proteids of the blood are indiffusible through an animal membrane, they are found in considerable quantity in the lymph. And, again, if sugar be injected into the blood-stream, the amount of sugar in the lymph outside the capillary soon exceeds that in the blood within it; and this is contrary to the law of diffusion that when a crystalloid passes from the fluid on one side of a membrane into that on the other, the percentage of such substance in the latter cannot rise above its percentage in the former. Against the theory of filtration it may be said that whereas the passage of fluid through an ordinary filter is due to pressure and proportional to it, in the case of the formation of lymph, on the other hand, an increase of pressure in the blood-capillaries may or may not lead to an increased flow of lymph. For instance, if the chorda tympani nerve be stimulated after the exhibition of atropin, though the pressure in the capillary vessels is greatly increased there is no evidence of an increased flow of lymph. That is to say, that not only do the cells of the gland fail to secrete saliva, but apparently the increased flow of lymph through the gland necessary for the supply of the constituents of such secretion does not take place. Again, when an increase in the capillary pressure does lead to an increase in the flow of lymph, it is not always found that the increased flow is proportional to the pressure, which would be the case if it was

merely a matter of filtration. As an instance of this may be cited the effect of increasing the capillary pressure by venous obstruction and arterial dilatation respectively, the former causing a greater flow of lymph than the latter, and the difference being more than can be accounted for by the difference in the capillary pressure resulting in each case. And yet again, it is against the filtration theory that substances pass in both directions through the capillary wall; nutritive material passing from the blood into the lymph-spaces, while waste products pass in the opposite direction.

For all these reasons, then, the "vitalistic" theory of Heidenhain, who regarded the formation of lymph as virtually an act of secretion—the result of the vital activity of the epithelial cells of the capillary wall—was generally accepted until comparatively recently; it has now, however, been itself called in question and the older view of filtration revived. One of the strongest planks in the secretory platform was the effect on lymph formation of the so called "lymphagogues"—substances which when injected into the blood increased the production of lymph without materially affecting the arterial pressure. But according to Starling some of these, such as sugar, though they do not affect the arterial pressure, do, by drawing water from the tissues, raise the venous and thus the capillary pressure and so produce the conditions favourable for increased filtration. In the case of such substances as peptone and beef extract, which in no way increase the capillary pressure, and to whose action, therefore, this argument could not apply, he considers that they increase the permeability of the capillary wall by injuring the epithelial cells and so lead to an increased escape of lymph. But this is obviously merely conjectural in the absence of any direct evidence of such injury, and it is quite open to us to consider such increased permeability an evidence of increased secretory activity if we choose.

We may perhaps find a middle path between the opposing views by supposing that the epithelial cells of the capillary wall transmit the lymph from the blood to the lymph-spaces by virtue of a "vital" action resembling if not fundamentally identical with secretion, and that in this process osmosis and filtration play their parts; it being borne in mind the while that they are the servants of the cell rather than the cell the servant of them, and that it has the power, when necessary, of modifying or entirely abrogating their influence.

Œdema and Dropsy.—When lymph accumulates in the lymph-spaces in sufficient excess the condition of *œdema* results. Under some circumstances the larger serous sacs are the seat of the

accumulation, and when the peritoneal cavity is thus distended with fluid we have the condition of *ascites*. The cause of such accumulation of lymph might be referred to obstruction to the outflow by the efferent lymphatics; but in reality the lymphatic anastomoses are so complete that this is never the case, and dropsy invariably results from vascular changes. Of these venous obstruction is the commonest, producing its effect not only by an increase of capillary pressure in the part or parts affected, but through the changes in the capillary walls resulting from insufficient renewal of the blood circulating within them. Such venous obstruction is common in cases of heart disease, in which the return of blood to the right side of the heart is hindered. In Bright's disease of the kidneys œdema may result from injury to the vessel wall alone from defective composition of the blood, quite apart from pressure changes. In another form of œdema the effusion of lymph is inflammatory in origin, and of this pleurisy and pericarditis afford examples.

We now come to the consideration of certain organs which may be termed "glands" in the widest sense of the word, but which differ markedly from ordinary secreting glands in their structure. In fact, they are in reality in no way comparable with them—as little as the lymphatic glands already described. Like these, they contain a considerable amount of adenoid or reticular tissue, with leucocytes in the meshes, and amongst other functions they have that of the production of leucocytes to replace the worn out white corpuscles of the blood. In this respect they are allied, through their resemblance to the solitary follicles, Peyer's patches, and lymphatic glands, with the lymphatic system generally, and may conveniently, therefore, be described here. These "glands"—the spleen, the thymus, and the tonsils—are frequently included, together with the lymphatic glands, under the general title of "ductless glands," a rather unfortunate term as it includes also the supra-renal bodies, the thyroids, &c., organs possessing a characteristic glandular structure, except in so far as they have no efferent duct. They are thus more entitled to be called ductless glands than the spleen and thymus, which have no glandular characteristics at all in the ordinary restricted sense of the word; though it is none the less true that having no glandular alveoli, the spleen and thymus have no duct leading from them. Only to this extent, however, are they "ductless glands."

A better term for the organs we are about to describe is that of "blood-glands"—*i.e.*, glands concerned with the production or

destruction of blood-corpuscles, thus associating them with the red marrow of bones and lymphoid tissue generally. But we have no really satisfactory name for these organs as a class.

The Spleen.

The spleen is in man a somewhat reniform body placed between the stomach and the diaphragm on the left side. On section it is seen to possess a fibrous capsule dipping into the organ at the concave hilum and giving support to the blood-vessels, lymphatics and nerves entering or leaving it at this point. From the under surface of the capsule fibrous trabeculæ enter the substance of the spleen, in which they divide again and again to form an irregular supporting network which is best developed in the region of the hilum. Between the strands of the fibrous network, the substance of the spleen—the *splenic pulp* as it is called—shows up as a dark red parenchyma of pulpy consistence, studded over its surface with numerous lighter spots about the size of a pin head—the *Malpighian bodies.* Microscopically the *capsule* is invested externally with a layer of polygonal squamous cells, similar to those lining the rest of the peritoneal cavity. Beneath this is a thin layer of connective tissue containing both white and elastic fibres, forming the fibrous portion of the peritoneal sheath. Beneath this again is a yet deeper stratum for connective tissue—the capsule proper of the spleen—containing many non-striped muscular fibres. The amount of muscular tissue present varies in different animals, being considerable in the dog and cat, while it is much less in man. Through the presence of this muscular element, which is found also in the trabeculæ, the spleen is enabled to dilate and contract rhythmically, so that its size, and consequently the amount of blood in it, varies within considerable limits. To this we shall return presently.

The *trabeculæ* divide again and again to form an irregular network and bear within them blood-vessels, lymphatics and nerves, which enter or leave the organ at the hilum.

The *pulp* of the spleen between the trabeculæ consists of a network somewhat similar to that of adenoid tissue but possessing special characters of its own. It is represented by a basis of fibrillar reticulum covered with epithelial cells, which are, however, larger and coarser than those of ordinary adenoid tissue. They are branched nucleated cells with inter-communicating flange-like processes. The fibrous tissue of the trabecular framework is continuous with the fibrillar network of the spleen pulp,

the finer trabeculæ breaking up terminally into fibrils, while the larger ones give off a fringe of fibrils from their edges. In the meshes of the network of the splenic pulp are found various kinds of cells—(1) Red blood-corpuscles which give to the spleen its dark red or chocolate colour. Many of these are normal, while others are altered in shape, or may even be represented by pigment granules only; (2) a number of leucocytes or small round mono-nucleated cells with but little perinuclear protoplasm; (3) cells indistinguishable from the finely-granular large white corpuscles of the blood, possessing two or three nuclei and the power of amœboid movement; (4) larger cells, with it may be more nuclei, and containing in their perinuclear protoplasm red blood-corpuscles or pigment granules or some intermediate stage of the red cells' disintegration. These cells, like the last, are also amœboid, and differ from the others in being, so to speak, special to the situation. (5) Lastly, there are found in the spleen of young animals, and even it is said in that of adult animals after a considerable loss of blood, nucleated cells with hæmoglobin bearing perinuclear protoplasm—*hæmatoblasts* or young red corpuscles.

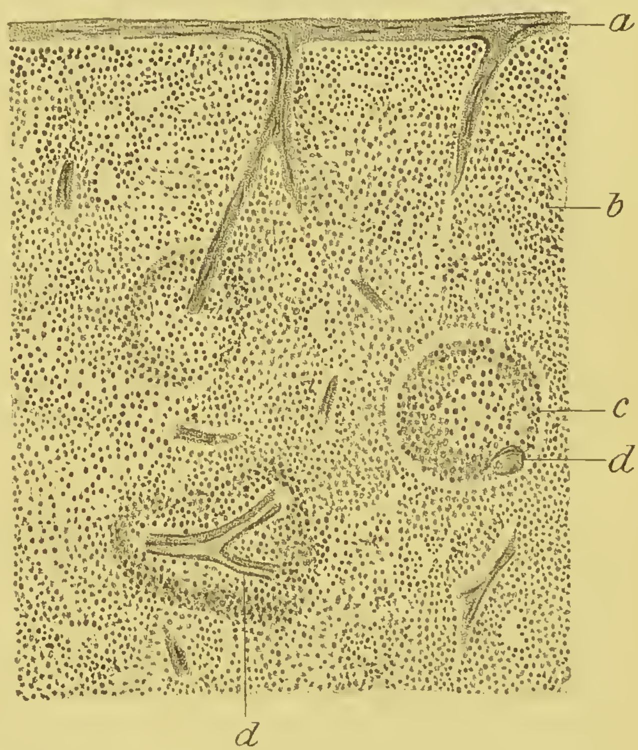

Fig. 259.—Section of Cat's Spleen.

a, Capsule, with trabeculæ passing into the substance of the spleen; *b*, pulp tissue; *c*, Malpighian or splenic corpuscle; *d*, artery in splenic corpuscle.

The *blood-vessels* of the spleen enter and leave it at the hilum. The arteries pass into the trabeculæ, in which they divide in correspondence with the trabecular divisions—small arterial twigs leaving the trabeculæ at intervals to plunge into the pulp tissue,

where they end in the following manner. The epithelial cells forming their walls are at first continuous with each other by their edges, and thus form a complete tube, but spaces presently appear between them, so that the tube is now perforated and communicates with the spaces between the cells of the splenic pulp. The cells of this incomplete vascular channel now anastomose with the cells of the splenic pulp, and thus the arterial twig becomes lost in the general parenchyma of the organ. The blood is collected into the veins in a similar way, the cells of the splenic pulp becoming arranged to form a tube with incomplete perforated sides, which further on becomes complete.

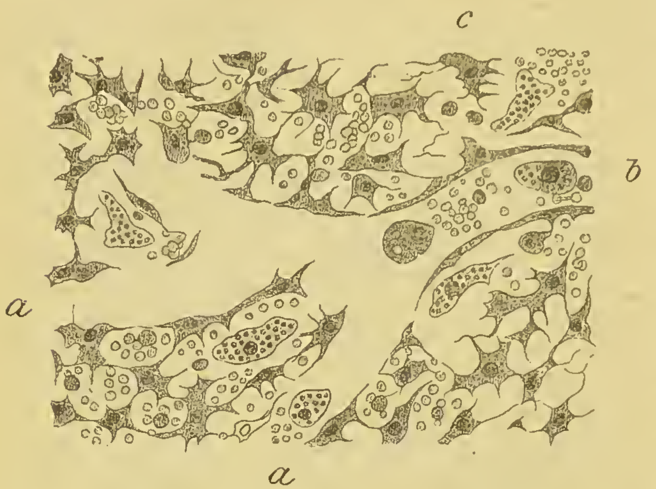

Fig. 260.—SECTION OF SHEEP'S SPLEEN (WASHED) SHOWING COMMENCEMENT OF VEINS IN PULP (× 300).

a, Commencing venous channels; *b*, venous radicle, with complete wall; *c*, cells of spleen pulp.

The venules thus formed quickly enter the trabeculæ and accompany the arteries to the hilum.

Lymphatics of the spleen.—There is a plexus of lymphatic channels in the capsule and trabeculæ from which the lymph is removed by lymphatic vessels leaving the organ at the hilum in company with the blood-vessels. The lymphatic relations of the small arterial branches in the splenic pulp, however, require special notice. As these vessels leave the trabeculæ and plunge into the pulp tissue their adventitia becomes converted to an adenoid sheath, which, increasing in quantity at intervals, gives rise to the rounded Malpighian bodies, which stand out on account of their lighter colour from the rest of the tissue on section of the organ. Sometimes the adenoid tissue is thus developed on one side of the vessel only, so that in transverse section the artery is seen to be placed eccentrically; in other cases evenly around it, when the vessel is seen in the centre of the lymphoid tissue. This special development of the adenoid sheath frequently takes place at the point where the arterial branch divides into two.

Under the microscope one of these nodules is seen to consist of the same kind of tissue as a solitary follicle, which it much resembles, but here, instead of the mass being surrounded with a lymph-sinus, the adenoid reticulum becomes at its periphery directly continuous with the coarser network of the splenic pulp; while the capillary network springing from the arterial twig and traversing the lymphoid tissue opens directly into the spaces between the splenic cells. As in other lymphoid tissue, the meshes of the adenoid reticulum of one of these Malpighian bodies are crowded with lymph-cells, and the blood flowing through the capillary network is subject to their influence on its way to join the blood of the splenic pulp generally; so that a certain proportion of the blood entering the spleen traverses this lymphoid tissue before it reaches the pulp.

The lymphatic spaces of the Malpighian bodies are in connection with the lymphatics of the trabeculæ from which the arterial twigs spring.

The nerves of the spleen.—The splenic nerves are derived from the solar plexus. The fibres start from a centre in the medulla, and passing down the cord leave it in the dorsal region by the left splanchnic, in which they pass to the semilunar ganglion and thence to the spleen. If these nerves be divided, an increase in the size of the organ results from the removal of the tonic influence they normally exercise over the non-striped muscle of the arteries, capsule and trabeculæ; on the other hand, if the peripheral cut ends are stimulated, contraction of the spleen ensues. Stimulation of the centre in the medulla, either by electricity or venous blood, has the same effect, and consequently in cases of asphyxia the spleen is found contracted. Stimulation of the fibres in the cord also contracts the organ, and a similar result ensues on stimulation of the lower cut ends of the vagi or splanchnics. Contraction may also be brought about reflexly by stimulation of the upper ends of the cut vagi as long as the splanchnics are undivided, as also by stimulation of such a sensory nerve as the sciatic. In the latter case, however, contraction will take place when both the vagi and the splanchnics are cut, so that the impulse in this case reaches the spleen by some other path.

The nerve-fibres are no doubt distributed to the muscle-fibres of the vessel walls as well as to those of the capsule and trabeculæ.

The spleen may also be stimulated to contraction directly by cold, electricity and the administration of quinine.

Changes in volume.—The spleen varies in size considerably at different parts of the day, according to the stages of the digestive processes, and it also frequently exhibits smaller rhythmical

contractions and dilatations. It increases in size after a meal, being at its largest at the end of five hours—that is to say, after gastric digestion and dilatation of the gastric vessels is at an end. This increase in size is due to a relaxation of the muscular fibres of the arteries of the spleen, and of the capsule and trabeculæ, due to inhibition of the ordinary tonic constricting influence exercised upon them through the splenic nerves.

The "splenic curve," showing the smaller rhythmical changes in the size of the spleen, is obtained by enclosing the organ in a Roy's oncometer constructed on the principle of the plethysmograph. The large curves in such a tracing are due to the rhythmical changes in the size of the organ, while the smaller curves are respiratory, the beat of the heart itself being sometimes recorded upon them. In the cat and dog the rhythmical contractions last about a minute and continue after section of the splenic nerves.

Chemistry of the spleen.—In addition to substances common to most organs, the spleen contains an iron-holding proteid and pigments such as hæmatin, associated with changes in the hæmoglobin of the broken-down blood-corpuscles. Among the extractives obtainable are found xanthin, hypoxanthin, leucin, and uric acid, indicative of nitrogenous metabolic activity.

Functions of the spleen.—One of these is undoubtedly the formation of white blood-corpuscles, for the blood of the splenic vein contains these in unusual amount. Furthermore, in the disease known as leucocythæmia, in which white corpuscles are present in the blood in greatly increased quantity, the spleen is found to be hypertrophied and the splenic or Malpighian corpuscles markedly increased in size. When the spleen is removed, too, the lymphatic glands in the body generally undergo hypertrophy, and one of the main functions of these we know to be the production of leucocytes. Secondly, the spleen, in some animals at least, is undoubtedly concerned in the production of coloured corpuscles, as shown by the presence of hæmatoblasts in the meshes of the splenic pulp. If the spleen in such animals be removed the red marrow of the bones is said to undergo hypertrophy. Thirdly, red blood-corpuscles are destroyed by the spleen, as evidenced by the iron-holding proteid and the pigments derived from hæmoglobin; the disintegrating blood-corpuscles in the protoplasm of the large white cells as already described; the accumulation of iron in the spleen in cases of pernicious anæmia, in which there is great destruction of the red cells. In connection with the destruction of the red blood-corpuscles in the spleen, it must be noted that free hæmoglobin does not occur in the blood

of the splenic vein, so that the materials required for the formation of bilirubin by the liver reach that organ in some other form.

Lastly, the presence of uric acid and the other extractives mentioned points to the part the spleen plays in nitrogenous metabolism, to which we shall refer later.

The Thymus Gland.

The thymus, like the spleen, may be termed a blood-gland, but we have not much knowledge of its precise function. It is an organ whose work is concerned with the earlier phases of life as it is at its largest a year or two after birth, after which it gradually atrophies and ultimately becomes entirely replaced by fat and connective tissue. During the time of its functional activity, *i.e.*, during fœtal life, and for some little time after birth it is composed almost entirely of lymphoid tissue, and thus no doubt takes its share in the production of white blood-corpuscles. At the same time, though it thus resembles the lymphatic glands and other collections of lymphoid tissue, the limit to its time of activity marks it out as being in some special manner concerned with the economy of the organism in its earlier stages of development.

The thymus is found as a long narrow body, somewhat reddish in colour, lying in the anterior mediastinum behind the sternum. The history of its development is distinctly peculiar to it. It commences as an outgrowth of the epithelium of the visceral clefts, the tubes of epithelial cells dividing dicrotonously to form an organ with the usual lobular arrangement of its parts; and this is accompanied with a proliferation of the gland cells, so that a system of solid tubes without a lumen results. The connective tissue in which the tubes lie rapidly assumes a lymphoid character, the whole being invested with a condensation of ordinary connective tissue. In time the epithelial tube becomes almost entirely removed, the lymphoid tissue growing at its expense. At a later stage in the history of the organ the lymphoid tissue itself degenerates and becomes converted to adipose tissue, which, however, retains the lobulated arrangement on which the organ was at first constructed. The following description is of the thymus in its period of functional activity, that is in its lymphoid stage, before the fatty change has supervened.

The thymus is invested with a fibrous capsule from which septa pass into its interior, dividing it into lobules; and from these primary septa subdivisions arise which partially divide the lobules into follicles. A lobule is shown in the accompanying

illustration, and as the whole gland is made up merely of a collection of these, a description of the structure of one of them will give the key to the structure of the whole organ. Such a lobule is usually pyramidal in shape, and on section exhibits a *cortex*, composed of a series of lymph-nodules, separated peripherally from each other by septa passing inwards from the capsule, but united at their bases where they join with the common central stem or *medulla.* Both the cortex and medulla consist of lymphoid tissue, which, however, differs somewhat in character in the two parts. Thus in the cortex the meshes of the adenoid reticulum are small and crowded with leucocytes, as in the case of the lymph follicular tissue of a lymphatic gland; while in the medulla the network is more open, and there are fewer cells, and many of these show mitotic changes. For these reasons the cortex stains more deeply than the medulla.

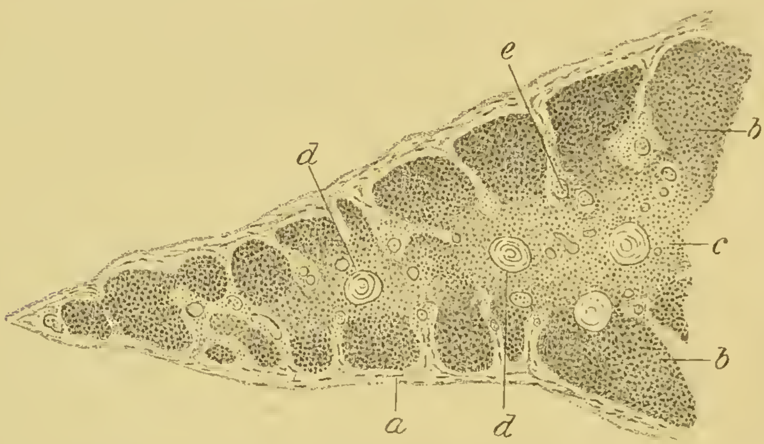

Fig. 261.—Section of Lobule of Thymus Gland of Young Child.

a, Fibrous investment of lobule; *b*, cortex; *c*, medulla; *d*, Hassall's corpuscles; *e*, blood-vessels.

In the latter are to be seen scattered here and there groups of cells arranged concentrically around a granular or corneous centre, and these are called Hassall's corpuscles. They represent the remains of the original epithelial tube which formed the foundation of the gland in its earliest stages. They were once supposed to be the remains of occluded blood-vessels, but this has been clearly disproved by Gulland.

The function of the gland, as before stated, is connected with the production of leucocytes. No fatal effects follow its removal in most animals, but in the frog, in which it persists throughout

life, its removal is said to cause death. Muscular tremors follow its removal, going on to paralysis accompanied with trophic disturbances, hydremia, &c. Intravascular injection of extract of the gland of the ox or man causes, like thyroid extract, a lowering of the blood-pressure, accompanied, it may be, with acceleration of the heart.

In hibernating animals it also seems to have some permanent function throughout life, becoming laden with fat as each period of hibernation is approached. Chemically, it is remarkable for the amount of nucleo-proteid it contains, and it is used as a source of this substance when it is required for injection with a view to the production of intravascular clotting. Like the spleen, it is rich in extractives—xanthin, hypoxanthin, leucin and succinic acid.

The Tonsils.

Placed on either side of the fauces, the tonsils consist of aggregations of lymphoid nodules lying immediately below the epithelial lining. The nodules are imbedded in a less dense adenoid tissue which reaches to the epithelium, the whole being marked off from the subjacent parts by a fibrous investment. Ten to fifteen orifices opening on the surface of the tonsilar projection lead to crypts formed by an outpushing of the epithelial layer between the subjacent lymph nodules, and into the lower ends of these crypts open the ducts of mucous glands. The stratified squamous epithelium, where it lies over a lymph nodule, is often "eroded" below from penetration of leucocytes on their way to the cavity of the mouth, into which they are discharged to mix with the saliva, where they form salivary corpuscles. Owing to this erosion, the sharp line usually seen at the junction of the dermis and epidermis is obscured.

The tonsils are in no way essential to the economy of the body and are frequently removed for comparatively trivial causes.

Hæmolymph Glands.

Before leaving the consideration of the blood-glands, reference must be made to certain structures first described by Robertson, and named by him "hæmolymph glands," which are found in the prevertebral fat of man and many other animals. These organs are numerous and small, varying in size from a pin's head to that of a small pea, dark chocolate in colour, of a very pulpy consistence, and occur in the course of small blood-vessels. They are

invested with a thin fibrous capsule immediately surrounding a peripheral sinus structurally resembling that of a lymphatic gland. That is to say, it is traversed by a coarse adenoid reticulum, but here the spaces of the network are occupied not by lymph, but by blood. Within this sinus is the body of the organ, consisting of a mass of lymphoid tissue, with large, more or less circular sinuses in it containing blood. These central spaces, however, do not exhibit an adenoid reticulum crossing them. The inner surface of the capsule and the surfaces of the lymph follicular tissue are covered by flattened epithelial cells.

No doubt the sinuses, both peripheral and central, are in direct connection with the afferent and efferent blood-vessels, and thus form a vascular dilatation.

With regard to function, two views have been suggested—(1) That the glands are concerned with the production of red blood-corpuscles, and (2) that they destroy the worn-out red cells. If a cover-glass preparation be made of the semi-fluid contents by smearing a cover-glass with the cut surface of the organ, cells resembling the large white cells of the spleen, and containing, like them, red corpuscles in their perinuclear protoplasm, may be readily demonstrated in large numbers; and the first of the two views mentioned supposes that this is a case of development of hæmoglobin-bearing spherules in the protoplasm, afterwards to be discharged from the cells as red blood-corpuscles, while the second view assumes that the white cells have ingested the red previous to their destruction.

We may now pass to the consideration of the true ductless glands, under which heading may be included the thyroid, the suprarenal capsules and the pituitary body; organs which, in contra-distinction to those just described, possess many of the morphological characters of secreting glands, with the important exception that they possess no duct. Being without a duct they produce no secretion destined to be poured out upon any of the surfaces of the body—no "external secretion," as it is called—which would bring them into line with an ordinary secreting gland such as the submaxillary; but they produce an "internal secretion"* which is of importance to the economy, so much so that death, after a longer or shorter interval, follows their removal or incompetence from disease. In this, however, they

* In the widest sense of the words, every tissue of the body may be regarded as producing an internal secretion, as it takes up substances from the blood and returns them to it in some form, *i.e.*, the essential nature of the act is obviously the same as in the case of glands. It is more convenient, however, to employ the term "internal secretion" in connection with glandular organs only.

do not differ from true glands with ducts, such as the liver and pancreas, in which the internal secretion may be more important than the external. This is eminently the case with the pancreas. If the pancreatic juice—the external secretion of the gland—be diverted from the intestine, life may still be maintained though the absorption of fat may be interfered with; but removal of the pancreas itself is fatal, as the organism is deprived of the substances the gland normally secretes, not into its ducts, but into the blood-stream. The importance of this internal secretion may readily be demonstrated experimentally by removing all but a fragment of the organ and transplanting the remaining fragment to another part of the body. In this case no external secretion of pancreatic juice is possible, but the presence of a portion of the gland, which is still in a position to maintain the usual exchange between it and the blood, is sufficient to save the situation and render a continuation of life possible. In other words, the pancreas and many other glands have a metabolic significance to the general economy of the organism quite apart from the special work assigned to their external secretion; and removal of one of them leads to a disorganisation of the metabolism of the body—in the case of the pancreas, an increase in the production of sugar being the result.

Even the kidneys, which at first sight one might be inclined to regard as likely to be concerned with excretion alone, have a very important metabolic relation with the rest of the body, and if one of them be removed and the greater part of the other the disturbance of the metabolism of the body generally is marked by polyuria and an increased excretion of urea (Bradford).

The liver is obviously a shining example of a gland with an important internal secretion, as both sugar and urea pass out of its cells, not into the lumina of the gland tubules, but into the blood. And here again, as with the pancreas, the internal secretion is of more importance to the organism than the external, for an animal can still live though the bile be carried out of the body through a biliary fistula, but it could not afford to sacrifice the power of the liver cells to secrete sugar and urea into the blood.

But all glands have not an equal importance in the matter of internal secretion. Thus the salivary glands may be removed without the general metabolism being affected, nor does the removal of the gastric or mammary glands have any distinct effect.

In the ductless glands, however, we have to deal with organs with no external secretion discharged through a duct, and, as we should expect, we find their relation to the general metabolism of considerable importance.

The Thyroid Gland.

The thyroid gland, situated in the neck, possesses two lateral lobes joined together by an isthmus of gland substance crossing in front of the trachea. It develops as a bilobed evagination from the anterior part of the alimentary canal in much the same way as the lungs, and thus has a considerable claim to be regarded morphologically as a true gland. The connection with the alimentary canal, however, is soon obliterated, and the organ, as we study it at a later stage, consists of a mass of isolated closed vesicles imbedded in connective tissue and enclosed in a fibrous capsule. The connective tissue septa contain many blood-vessels, lymphatics and nerves, the vascular supply being peculiarly liberal. The gland vesicles themselves are large and round or oblong in shape, and lined by a single layer of cubical epithelial cells, the space they enclose containing, in the fresh state, a glairy mucinous fluid. The latter, however, is sometimes, and indeed frequently, replaced by a more solid colloid material.

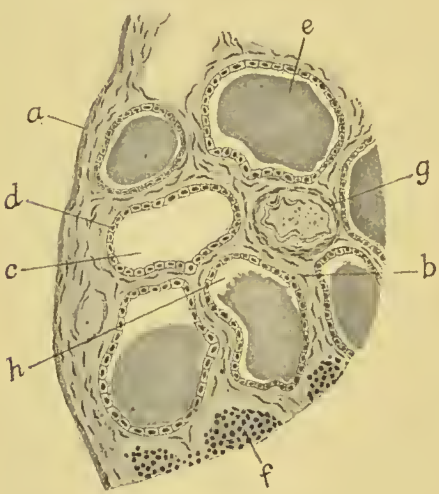

Fig. 262.—Section of Thyroid (Human).

a, Capsule; *b*, fibrous septa; *c*, alveolus lined with cubical cells, *d*; *e*, homogeneous contents of alveoli; *f*, surface view of alveolus; *g*, artery; *h*, irregular outline of retracted contents of alveolus.

The functions of this organ are not very well known to us. In man and monkeys removal of it leads to a condition resembling the disease known as myxœdema, in which there is hyperplasia of the subcutaneous connective tissue, associated with tremors and twitchings, slowness of mind and body, &c. In the case of carnivors the operation is frequently followed by symptoms of central nervous derangement, evidenced by muscular spasms or even convulsions and disorders of general nutrition, followed by death before the myxœdematous change in the skin has time to develop.

Cretinism in children and myxœdema in adults are both the result of disease of the thyroid gland.

It is to be noted that, as in the case of the pancreas, so here, if a piece of the gland be grafted in another part of the body, or if on removal a portion of the gland be left *in situ*, no evil effects necessarily result, the grafted or remaining portion sufficing to provide the necessary secretion for the maintenance of the normal metabolism of the organism. Furthermore, injection of thyroid extract subcutaneously, and even feeding with the gland itself, will remove the myxœdematous condition after it has once supervened, though of course the treatment requires to be persisted in throughout life. The thyroid, therefore, may be regarded as producing some substance of the first importance in the maintenance of the normal metabolism of the body, and apparently particularly of the central nervous system, but what the precise nature of the substance is is at present quite uncertain. According to some it is a nucleo-proteid, and according to others an iodine-containing compound — thyro-iodine—which has been extracted from the gland.

The thyroid gland probably not only produces substances beneficial to the organism but has the function of destroying toxic bodies. The intravascular injection of thyro-iodine causes a fall of blood-pressure by raising the excitability of the vagus and depressor fibres to the heart and lowering that of the augmentor and vaso-constrictor fibres, and the fall of blood-pressure is partly due to slowing of the heart and partly to dilatation of the vessels. On the other hand, sodium iodide and similar neutral salts of iodine raise the blood-pressure by paralysing the vagus and depressor fibres and increasing the excitability of the augmentors and vaso-constrictors. It has therefore been suggested that one function of the thyroid is to cause the iodine salts taken into the body, which would otherwise be harmful, to enter into organic combination, the resulting thyro-iodine exerting a beneficial instead of a deleterious effect upon the vascular mechanism.

So far as the colloid contents of the vesicles are concerned, the secretion of the gland is obviously not a true internal but a quasi-external one; for the glairy or colloid material is discharged from the cells lining the vesicles into the cavities of the same precisely in the way that the external secretion of any gland is discharged into the lumen of its tubules. Nor does it appear that after returning through the wall of the vesicle it passes directly into the blood-stream, as it is found filling the lymphatic spaces, often of large size, in the connective tissue septa. In its return through the epithelial wall it passes probably between the cells and not through them, for when, as in hardened specimens, the vesicular contents are found retracted from the epithelial lining, delicate threads of colloid material may be traced from the main mass to the points of junction between the several cells.

Recent experiments carried out by Swale-Vincent and Jolly have thrown much doubt on the exact functions of the gland, as after complete removal in various classes of animals they failed to obtain any phenomena characteristic of the myxomatous condition; indeed, in the light of these experiments, any decided statement of their probable function can hardly be formulated.

The Suprarenal Bodies.

The suprarenal bodies, or capsules, as they are sometimes called, are developed in the mesoblast and not in the form of outgrowths from the alimentary canal, and their glandular characteristics are more obvious in their later than in their earlier stages. No organ exhibits such variations in structure in different animals. Thus in some amphibians the cortex and medulla are entirely separated from each other; in birds (common fowl) they are intermingled in the form of a network; while in the mammalia the cortex surrounds the medulla in the usual manner. But not only are there differences between these great classes, but distinct, though minor, differences are to be observed between the glands of different species of the same class; so that the suprarenals of the cat, horse and sheep each present marked features peculiar to themselves which enable us to readily recognise them under the microscope. We cannot here, however, consider varieties in the structure of these remarkable and interesting organs in the different species, but must confine our attention to the mammalian gland, of which the sheep affords us an illustrative example.

The suprarenal gland of the sheep is a somewhat round or reniform body lying in the perirenal fat. On section it shows a division into a lighter cortex and more deeply coloured medulla, the former constituting the main mass of the organ, and everywhere enveloping the medulla except at the hilum, where the latter reaches the surface. The whole organ is surrounded by a fibrous capsule sending in delicate septa containing blood-vessels which pass inwards from the periphery to the centre of the medulla. Here they terminate in a large efferent venous channel lined with simple squamous epithelium surrounded with a layer of fibrous tissue; a channel which extends through the medulla and ends in the efferent vein at the hilum. The greater part of the cortex consists of a system of radially arranged columns of cells with lateral anastomosing cords, forming a network resembling that of a liver lobule. The cells are pentagonal or polygonal in shape,

often two abreast, and glandular in character, possessing a nucleus and nucleolus. To this part of the cortex the name

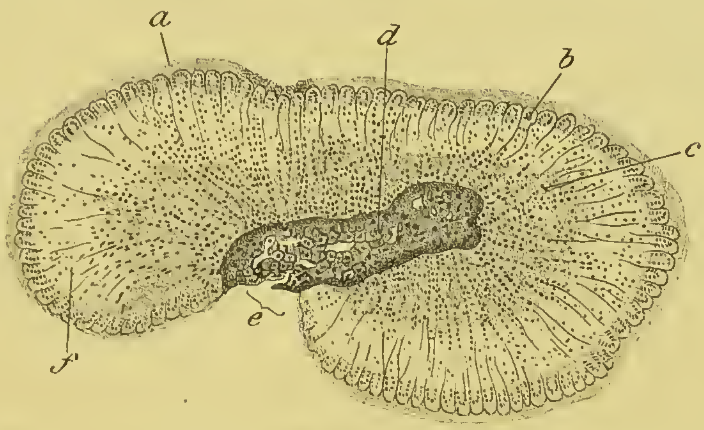

Fig. 263.—LONGITUDINAL SECTION OF SUPRARENAL GLAND OF CAT.
a, Capsule; *b*, zona glomerulosa of cortex; *c*, zona fasciculata of cortex; *d*, medulla; *e*, hilum; *f*, zone of enlarged cells in zona fasciculata.

zona fasciculata is applied, and if it be traced towards the periphery it is seen to terminate beneath the capsule in the *zona glomerulosa*, which forms about one-fifth of the whole cortex in breadth, and consists of a number of alveoli, round, oblong or convoluted in outline. These alveoli are lined by polygonal granular nucleated cells, surrounding a lumen, into which they may project so far as to meet in the middle of it. Usually, however, the lumen is quite distinct. At the point where the zona glomerulosa and fasciculata meet, the alveoli of the former are directly continuous with the solid cords of the latter, of which they seem to form the expanded extremities.

Fig. 264.—SECTION OF SUPRARENAL GLAND OF SHEEP (SHOWING ALVEOLI OF ZONA GLOMERULOSA) (× 300).
a, Alveolus; *b*, capillary wall.

If the zona fasciculata be followed in the other direction, towards the medulla, the columns of cells are seen to lose their radial and columnar formation and form

a network—the *zona reticularis*—which becomes less open, *i.e.*, with smaller intervening capillary spaces, as the inner edge of the cortex is reached. These capillary spaces are continuous with similar ones between the radial columns of cells in the zona fasciculata, and these again may be followed outwards till they join those in the delicate connective tissue septa sent in from the capsule between the alveoli of the zona glomerulosa.

The medulla, which is sharply marked off from the cortex and apparently only connected with it through the medium of the capillaries passing between the two, consists of a number of somewhat tortuous convoluted tubules, considerably broader than the cords of cells in the zona fasciculata, and separated from each other by a vascular network continuous with that of the cortex. The spaces between the gland tubes, however, are not

Fig. 265.—Section of Suprarenal Gland of Sheep (showing Junction of Cortex and Medulla) (× 200).

a, Cortex; *b*, medulla; *c*, capillary blood-vessel.

tubular, as blood-capillaries generally are, but quite irregular, their shape depending on the outlines of the tubes between which they lie. The walls of these vascular channels are formed, like those of the capillaries of the cortex, of a layer of squamous cells closely applied to the surfaces of the gland alveoli.

The alveoli of the medulla have no very obvious lumen, and are lined by tall columnar cells, the inner ends of which meet each other in the centre; the nuclei of the cells being, not as is usually

the case, placed towards their basal end, but in their inner free extremity (Fig. 265). The blood from the interalveolar spaces is received into the large efferent venous channel in the centre of the medulla—a passage lined with squamous epithelium and surrounded with a layer of fibrous tissues. This channel extends through the length of the medulla and opens into the efferent vein of the gland at the hilum. Here and there between the alveoli may be seen sections of non-medullated nerve-bundles and small blood-vessels supported by delicate connective tissue.

The suprarenal gland of man may be regarded as having earned for the organ generally the title of "capsule." It fits the upper end of the kidney as a kind of cap, and on section is somewhat tri-radiate in shape. The zona fasciculata is well marked, but the columns of cells do not communicate laterally with each other so freely as in many other animals; nor does the zona glomerulosa exhibit a series of distinct alveoli with a well-marked lumen, so well seen in the gland of the sheep, but rather a series of somewhat irregular clusters of cells, which have given the name "glomerulosa" to this part of the cortex. From these clusters of cells in man we may pass through intermediate stages in the horse, cat, dog and other mammals up to the distinct alveoli in the sheep, which no doubt represents the common type.

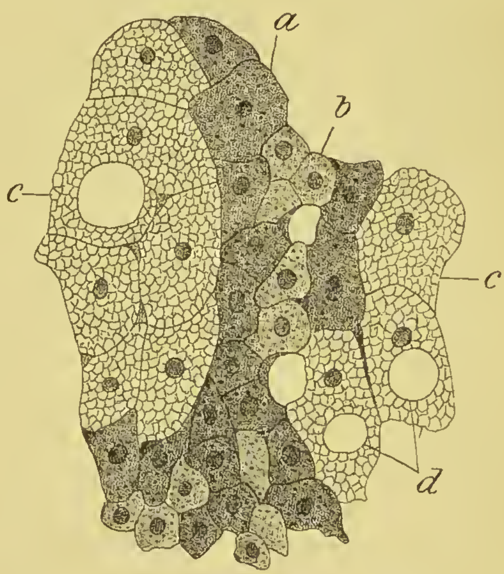

Fig. 266.—Section of Suprarenal Gland of Cat (× 350).

a, Unaltered cells of zona fasciculata (outer part); *b*, cells coloured normally a golden yellow; *c*, enlarged unstained cells, showing fat globules and intracellular network: *d*, fat globules, unstained.

The cells of the cortex and medulla of the suprarenal bodies exhibit changes no doubt associated with their functional activity, but these changes seem to occur in a very varying degree in different species, nor has their significance yet been determined. One very obvious alteration occurs typically in the suprarenal of the cat—the cells of the outer third of the zona fasciculata enlarge, often to the extent of twice or thrice their original size, refuse to stain

with ordinary reagents, and exhibit a very distinct intracellular network; and these changes, as we have seen in the case of other gland cells, are often distinctive of the so-called "resting" stage, when the cell is elaborating the material of its secretion. A section of such a suprarenal gland stained with hæmatoxylin reveals under a low power of the microscope the appearance of an unstained band lying immediately within the zona glomerulosa (Fig. 266). Secondly, the cells of the zona glomerulosa of the sheep frequently exhibit in their interior numerous well-marked granules which stain dark brown with osmic acid, and similar, but smaller, granules are to be found in the cells of other parts of the organ. Thirdly, in the suprarenals of most animals, and notably in those of the cat, the cells, especially of the zona fasciculata and the medulla, exhibit large globules, said to be of a fatty nature, which frequently distend them, the nucleus being pushed to one side. Fourthly, the medulla of the gland in various species often shows marked pigmentation, which is said to be due to the action of the chromium salt used in preparing the tissue for section.

The history of the development of the suprarenal bodies is interesting. The medulla is stated to be developed from the sympathetic nervous system, while the cortex is developed from the mesoblastic tissue in the neighbourhood of the large blood-vessels in front of the spinal column. To what extent it is a fact that the medulla has the origin assigned to it, it might be well at present to regard as undecided, but that the organ in its development is intimately associated with the sympathetic ganglia is indubitable, and is clearly seen in transverse sections of embryo rats and other mammals, in which well-marked strands pass from the ganglia and plunge into the suprarenal substance.

With regard to the functions of the glands, our knowledge so far is that of the result of their removal experimentally or their incompetence through disease, and of the injection of extracts of their substance into the blood-stream. In Addison's disease, in which the suprarenals undergo tubercular destruction (commencing in the medulla), muscular weakness and pigmentation of the skin, or "bronzing" as it is termed, precede death, and death also follows extirpation of the gland in animals. The experiments of Oliver and Schäfer on injection of extract of the medulla of the organ into the veins have been very instructive. When a small quantity of a watery extract of dry medulla of the gland is injected into the blood a remarkable rise in blood-pressure at once results. This might be ascribed either to a change in the force or speed of the cardiac action or to variation in the calibre of the systemic vessels, and both factors are apparently concerned in

the change. If the vagi be left uncut, so that the connections of the heart with the cardio-inhibitory centre remain intact, the rise in pressure is almost entirely due to the arterial constriction which immediately follows the injection, as in this instance the heart slows, apparently from the action of the drug on the cardio-inhibitory centre, as the same effect does not occur after the nerves are divided, or the central nervous system destroyed. A very simple method of ascertaining the results of injection is to take a frog, pith it, and make two openings into the circulation—*e.g.*, one into the sinus and the other into the ventricle; the former as an outlet and the latter an inlet to a stream of fluid perfused through the vessels. To obtain an index from which we can note the effects of the extract, it is advisable to perfuse through the vessels a stream of saline, noting carefully the pressure of the fluid, and collecting the amount passing through the circulation in a given time; the extract is then perfused in place of the saline, when it will be observed that the flow from the vessels decreases greatly in amount, from the constriction of the vessels that at once occurs. From the previous destruction of the central system it is obvious that the constriction must be due either to a direct stimulation of the muscular fibres of the arteries or a specific action of the drug on the vaso-constrictor terminals, and from recent investigations on this point by Dixon and others it would seem to be the latter, for if a solution of apocodeine be first transfused through the arteries the constriction does not occur. If the extract be injected into an animal in which the vagi have been divided, the rise in blood-pressure is very marked indeed, as we not only have the general constriction of the vessels but also a pronounced acceleration of the cardiac rhythm with a distinct increase in force. From the peculiar action of the extract on the vessels, the active principle adrenalin is an invaluable drug in persistent hæmorrhages, where it may be painted or sprayed over the bleeding area. The action of the secretion is probably not confined to cardiac and arterial muscle, for if the solution be applied directly to ordinary skeletal muscle an effect is produced on the contraction curve closely resembling that of veratrine, though the prolongation of the relaxation period is hardly so pronounced. The function of the gland would therefore appear to be to secrete a substance which preserves the tonicity of the muscle of the heart and arteries more especially, with, however, a similar, though less pronounced, influence on the general musculature of the body. As in the case of the thyroid, toxic bodies are probably destroyed or neutralised in the gland, and thus rendered either harmless or even beneficial to the tissues. The

medulla only of the glands is effective, and a benzoyl compound has been obtained from it which causes the rise in blood-pressure. It is an alkaloidal base with the formula $C_{17}H_{15}NO_4$, and has been named by Abel *epinephrin.*

The Pituitary Body.

The posterior lobe arising as a diverticulum from the epithelium of the mouth need only be considered here, the anterior lobe being developed from the central nervous system. The posterior lobe consists of a number of round, oval or elongated alveoli, formed of columnar or polygonal cells which do not usually surround a lumen. When such a lumen exists it may contain colloid material similar to that of the alveoli of the thyroid gland. Between the columnar or polygonal cells, spindle-shaped cells are found here and there. The lobe is surrounded with a fibrous envelope which sends in interalveolar septa supporting a network of capillaries, &c.

With regard to the function of the organ, we again can do little more than record the result of disease, experimental removal, and the injection into the blood-stream of gland extracts. Disease of the pituitary body is followed not by myxœdema, as in the case of the thyroid, but by the condition of acromegaly, the bones of the face and limbs becoming thickened. Removal of the organ in carnivora has been followed by death within fourteen days, with symptoms of muscular weakness, tremors, &c., similar to those following excision of the thyroid. Here again, as in the case of suprarenals, only part of the gland seems to afford extracts affecting the vascular mechanism when injected into the blood-stream. Extracts of the anterior lobe or hypophysis have no effect. The posterior lobe or infundibular body yields two substances, one of which when injected directly constricts the arterioles and increases the force of the heart-beat, thus raising the blood-pressure, and so has a *pressor* effect; while the other causes a fall in the pressure, and thus has a *depressor* effect. The latter will produce its effect even when injected after a rise has been obtained by previous injection of the pressor substance.

CHAPTER XI.

ABSORPTION.

In the preceding chapter we have considered briefly the question of the nature and causes of the transudation of lymph and the physical and vitalistic theories in connection with the same, and we may now the more advantageously approach the consideration of the absorption of food from the alimentary canal. We shall find that here also, as in the case of the passage of lymph through the walls of the capillary vessels, we have to balance the forces—physical and vital—and endeavour to assign to each their relative importance and proper rôle.

We have seen that, speaking generally, digestion consists in the conversion of ordinary indiffusible proteids into diffusible peptone, of starch into diffusible sugar, and in the emulsification of fats whereby the original fatty globules are split up into minute particles. With the exception of fat, absorption of these substances occurs in the stomach at an early stage of digestion, for it must not be supposed for a moment that absorption is postponed until digestion is completed. On the contrary, they overlap, absorption commencing virtually with digestion, increasing as the latter proceeds, and continuing after it is finished. Though absorption of rapidly diffusible substances generally and of diffusible peptones and sugar readily takes place in the stomach, yet the small intestine, with its immense absorptive area (increased by the valvulæ conniventes and the innumerable villi), is by far the most important in this relation, while in the large intestine mainly water and salts are absorbed. Fat is absorbed in the small intestine alone.

The peptone, sugar and fat thus absorbed might pass into the blood-current by either of two paths. They might enter the lacteals of the villi of the small intestine, be transmitted thence through the mesenteric lymphatic vessels and glands to the receptaculum chyli and thence by the thoracic duct to the subclavian vein at the root of the neck, or they might enter the blood-capillary system of the mucous membrane of the alimentary canal, in which case they

would be carried by the portal vein to the liver and subjected to the important influence of its metabolic activity before being passed on by the hepatic vein to the inferior vena cava. We need not at this point consider the action of the liver upon the food products which pass through it, a matter which will be dealt with when metabolism generally is under consideration, but may confine ourselves in this chapter to the question of the path taken by the several foodstuffs—proteids, carbohydrates and fats—and the mechanism of absorption in the different cases.

The course taken by the fats.—Fat differs from peptone, sugar and salts in being only absorbed in the intestine and not in the stomach also, and in the intestine the villi afford the fat-absorbing surface. After a meal containing fat, the lacteals of the mesentery contain

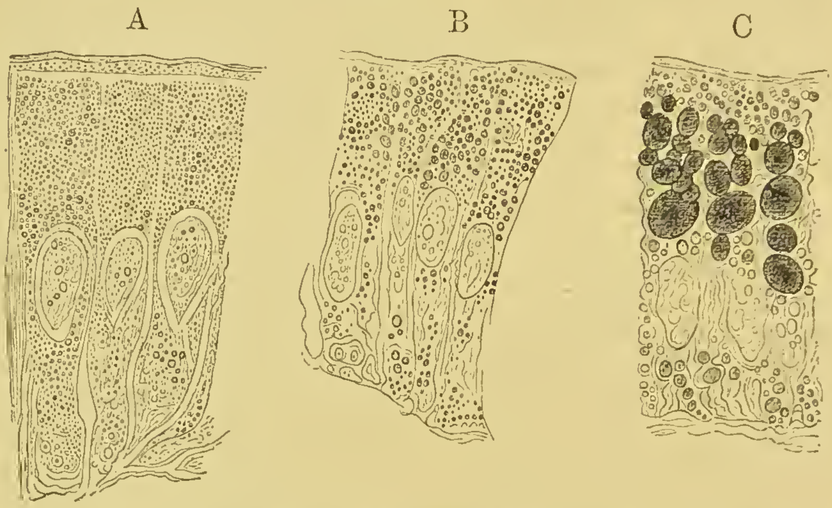

Fig. 267.—Fat Absorption in Intestinal Epithelium of Frog. (After Krehl.)

chyle on its way to the thoracic duct, and in this we have reason to conclude that fat enters the central lacteal of a villus after passing through the columnar epithelium covering it. But it does not follow that *all* the fat pursues this path, and in this connection it may be mentioned that there is a considerable difference in the amount of fat which may be collected from a cannula inserted in the thoracic duct and the amount taken at a meal—only about 60 per cent. of the fat ingested is recoverable in this manner, and this affords a *prima facie* reason for supposing that some might pass into the blood-capillaries of the villi and so into the portal circulation. There are, however, several reasons for supposing it does not and that we cannot account for the deficit in this way.

In the first place, though during digestion the blood of the portal vein contains a certain quantity of fat, yet it does not differ in this from the blood of the body generally, which is receiving fat through the thoracic duct, and in fact the blood of the carotid artery contains more fat than does that of the portal vein. Again, further evidence that the fat in the portal vein during digestion is received through the thoracic duct (*i.e.*, that the portal vein only shares in the fat poured into the vascular system at the root of the neck and does not receive it directly from the alimentary canal) is afforded by the fact that if the chyle in the thoracic duct be led outside the body, instead of being allowed to fall into the circulation in the usual way, the portal vein suffers with the rest of the vascular system in the loss of fat from the blood contained in it. Finally, the microscope confirms the view that the fat passes into the lacteals of the villi and not into the blood-capillaries. If a section be made of the small intestine of an animal which has been previously fed with fat, and stained with osmic acid, fat is to be found in the epithelial cells covering the villi, in the spaces of the reticular network, in the central lacteal vessel, even in the leucocytes, anywhere in fact except in the blood-capillaries.

The difference, therefore, between the amount of fat recoverable from the thoracic duct and the amount which has been ingested cannot be accounted for thus, and at present has not been explained. After excision of the pancreas, it may be noted, no fat is absorbed at all.

The course taken by water and salts.—The injection of water or normal saline into the intestine does not cause any increase in the flow in the thoracic duct, and from this it may be concluded that water is normally absorbed by the blood-capillaries. If, however, an *excess* of fluid be injected, the flow in the thoracic duct may be increased to some extent. With regard to the path pursued by the salts it is difficult to speak decisively, as they are quickly found both in the blood and in the thoracic duct after injection into the intestine. Probably they follow the course of the water for the most part, though they may to some extent pass into the lacteals of the villi.

The course taken by the sugar.—As the amount of sugar present in the blood and the chyle, small as it is, remains fairly constant and is not increased after a sugar-containing meal, while the blood of the portal vein contains an increased amount, we may conclude that sugar enters the circulation through the portal system and not through the lacteals of the villi.

The course of the proteids.—A difficulty here meets us in the fact that the proteid absorbed changes its character in its passage

through the mucosa of the alimentary canal and cannot be traced as peptone in the blood. This conversion of peptone to one of the ordinary proteids of the blood in its passage through the mucosa is well illustrated by the following experiment. If a loop of excised intestine be filled with peptone and artificial circulation maintained through the mesenteric vessels supplying it, the peptone will be absorbed and disappear as such, *i.e.*, it cannot be detected in the blood leaving the mesenteric vein. Nor can peptone be found in the chyle of the thoracic duct. We have, however, some indirect evidence that it passes into the portal circulation and not into the lacteals of the villi. The absorption of proteid food leads to an increase in the urea excreted by the kidneys, and a negative indication that the proteids follow the path suggested is afforded by the fact that if we exclude the possibility of its reaching the general circulation in the chyle by ligaturing the thoracic duct, an increase in the excretion of urea still follows a proteid meal. At the same time, we cannot say that it is impossible that any of the proteids passes into the lacteals. Moreover, in herbivora, into whose diet fat enters to a very small extent comparatively, the lacteals are well developed, and this one would hardly expect to be the case if they were concerned with the absorption of fat alone.

Mechanism of Absorption.

Absorption of fat.—The emulsified fat in the intestine passes through the epithelium covering the villi on its way to the meshes of the reticular network between the epithelium and the central lacteal. It certainly does not pass *between* the cells, a fact which may very readily be verified in an osmic acid preparation of the intestine, in which fat globules of various sizes may be seen to lie in the protoplasm of the columnar cells. No fat in such a preparation is seen in the cells of Lieberkühn's follicles.

We saw that under the digestive action of the pancreatic juice, aided to a certain extent by the bile, the ingested fat was partly broken down into glycerine and fatty acid, and partly retained in the form of a delicate emulsion with traces of soaps, which have probably assisted largely in the emulsification process, but the method in which the products pass through the intestinal wall is to a very large degree unknown. There are two chief theories—the Emulsification and the Solution. In the former it is believed that the fat is taken into the epithelial cell in the form of very finely divided fat, while in the latter it is supposed to be absorbed in as glycerine and fatty acid and transformed into fat in the cells covering the villus. Of the two, the second seems to be the more

probable, for if a kitten fed on cream be killed during absorption, and the cells stained with osmic acid, it will be found that there is a distinct zone immediately below the striated border of the cell, which apparently contains no fat globules, such as we would certainly have if the food material had been absorbed in the form of fat; again, if an animal be fed on fatty acid and glycerine, or even the former alone, fat globules are formed in the usual way in the cells; and, indeed, from recent experiments, it would seem as if the emulsification process, while certainly assisting in the process, can really be dispensed with entirely.

In discussing the absorption of diffusible substances we shall find that we are met with the consideration as to how far such absorption may be regarded as depending on the laws of diffusion alone, and as to whether these laws will account for the whole process; but here, in the case of the absorption of fat, the dependence of the cell on its so-called "vital" force for the work done is obvious on the face of it.

From the meshes of the reticular network within the villus the fatty particles find their way into the central lacteal, and in their passage through its wall undergo a change. They become more finely subdivided, so that in the interior of the lacteal we find, not as before, a number of fatty particles, some large and some small; but for the most part the fat is in an extremely fine form of subdivision, constituting the "molecular basis" of the chyle.

The passage of the fat from the epithelial cell to the central lacteal is generally ascribed to the leucocytes which are found in immense numbers in the reticulum of the villus during absorption; they are supposed to engulf the fatty body, but not to digest it, according to its ordinary custom, and then to carry it to the central lacteal, where the fatty burden is discharged into the chyle. The leucocytes can certainly be shown to contain fatty particles, though of course it is quite possible that the ingested fat is there merely to supply the demands of the cell itself. Certainly, to believe that the corpuscle travels to the epithelial cell to receive its load of fat, and that it then passes through the reticulum to the central lacteal, there to discharge the load, thereafter probably returning to the epithelium for more, very highly developed functional powers must be ascribed to the cells.

The process may, however, be an entirely mechanical one. When the fatty particles are extruded from the base of the epithelial cell into the interior of the villus they come very rapidly into contact with the lacteal wall, and the intervention of leucocytes is in no way needed. We say rapidly in this sense, that by the rhythmical contraction of the muscular fibres

of the villus during digestion the fatty particles are equally distributed in the lymph surrounding the lacteal; the muscle-fibres cause a movement analogous to that of churning in the interior of the villus, and thus the lymph, with its evenly distributed fatty particles, bathes the wall of the lacteal. Through this the fatty particles pass, because it is the nature of the cells forming the wall to cause them to do so—a "vital characteristic" to pass fat particles through them in that direction—just as it is one of their functions to complete the subdivision of the fatty particles into the "molecular basis" of the chyle.

That some of the leucocytes should contain fat droplets is only what one might expect from their character as general phagocytes, and such droplets might no doubt be intended for their own consumption.

The muscular fibres of the villus, in addition to their action already referred to, by their contraction empty the lacteal into the valved lymphatic vessels below, from which the chyle cannot return, and by their relaxation allow the villus and the lacteal to resume their original form and the process of refilling of the lacteal to take place.

Absorption of diffusible substances—peptone, sugar, salts, and water. These enter the capillary vessels, through the walls of which there is, as usual, a current in both directions, but more especially from without inwards—at least during the process of digestion. Inasmuch as these substances are diffusible, though in different degrees, it might at first sight be thought possible that the laws of diffusion alone would be sufficient to account for their passage through the columnar epithelium in the first place, and the capillary wall in the second, into the blood-stream, but on further investigation this view is found to be untenable. If a Thiry's fistula be made of a loop of the intestine and the rate of absorption of solutions of different strength be observed, it is found that this does not follow the laws which regulate the passage of such substances through an ordinary septum. Frequently a substance which will pass through an ordinary membrane more slowly than another will be absorbed by the intestine more quickly, and *vice versa.* This is not to say that diffusion does not play its part both in the case of the current from the blood to the intestinal lumen (secretion) and in the case of the current from the intestine to the blood (absorption), but rather that superadded to the influence of diffusion, and controlling and modifying it, we have to recognise the special vital force of the cell itself. This special activity of the cell itself is, no doubt, greater in the columnar-celled covering of the villi than in the

wall of the capillary vessel, which by its thinness predisposes one to regard it more readily as an ordinary diffusion membrane. If the portal blood-stream be examined, it will be found to contain no peptone, which, as we have seen, is the chief resultant of proteolytic digestion, but only the simple indiffusible serum-albumin and globulin. It is obvious, therefore, that a conversion of the one type to the other must have taken place somewhere in the mucous membrane. The process has been ascribed both to a functional power of the epithelial cells covering the villus and to the action of leucocytes, which are found in increased number in the tissues during absorption. If peptone solution be, however, passed through lymphatic glands or other tissues rich in leucocytes, the conversion does not occur, so that we would require a further specialisation of function of the intestinal leucocytes to account for the change. Taking all the factors into consideration, it seems most probable that the epithelial cells are the agents which effect the change. But in either case we must recognise something more than a diffusion membrane in the capillary wall, for if the peptone is converted to indiffusible proteid in the columnar epithelium, then the capillary wall has the power of giving passage to indiffusible substances.

But besides the results of experiments, there are other reasons for regarding the passage of solutions through cells, such as those lining the alimentary canal, as a distinctly vital rather than a mere physical act. In cases of nervous dyspepsia, diffusible substances such as peptone are not necessarily absorbed from the stomach, even though the lining membrane is not physically changed. These cases of dyspepsia are characterised by want of activity of the cells lining the stomach, both in the direction of secretion and absorption, and the want of activity is central in origin, that is to say, the normal nervous stimulus is not supplied from the brain. It is quite clear that the physiological processes of absorption and secretion, essential alike in their nature, which can thus be influenced through the nervous system, cannot depend on merely physical laws of diffusion and osmosis; rather the cells employ these laws, make use of them in the carrying out of their function, but never normally lose control over them.

Perhaps it is unnecessary to push the argument further, but another stumbling block to the theory of merely physical action is afforded by the "selective" power of the capillaries and lacteal of the villus. Apart from inherent tendency in the cells themselves, why should the capillaries receive the proteids, sugar, and salts, while the lacteal receives the fat? The laws of

diffusion and osmosis alone will in no way account for such selective results.

Though we have spoken of the columnar cells covering the villi as the agents of absorption of these diffusible substances, it must be borne in mind that they are also absorbed through the general lining of the stomach and small intestine, and to some extent probably through the epithelium of Lieberkühn's crypts.

CHAPTER XII.

EXCRETION.

WE have now considered the ingestion of food substances, the changes which these undergo in the alimentary canal, and their absorption into the blood. If we followed the natural course of events we should trace the absorbed substances into the tissues, from the tissues into the blood-stream again, and finally study the end products as they leave the organism. And this is certainly the order in which it would be advantageous to study events were our knowledge of the metabolic changes in the body—the steps by which the food is transformed into the waste substances excreted—in any sense complete and satisfactory. But research in this most difficult region of physiology is a matter of "broken lights" rather than a continuous story, and we do not touch certainty again until we deal with the end products themselves, which represent the food when its course is run and its history concluded. It is because our knowledge of these waste products is of service to the understanding of what little we know of the previous changes the food has undergone subsequent to its absorption from the alimentary canal that we shall now turn to Excretion, and defer till later the consideration of these changes under the heading of Metabolism.

The waste products of the body are eliminated by the kidneys, skin, lungs and liver. Excretion by the lungs we have already studied, and seen that by this channel the whole, or nearly the whole, of the carbonic acid and a considerable amount of the water escapes, and excretion in the fæces has also been dealt with, leaving the kidney and the skin for our present consideration. Of the main waste products of the organism, viz., urea, carbon dioxide, salts and water, the kidney discharges in the urine practically all the urea and allied bodies, nearly all the salts, and a large amount of the water, while the skin excretes a considerable, though varying, quantity of water, with a small quantity of salts and CO_2. The kidney thus represents the means of exit for the body's nitrogenous waste.

I.—Excretion by the Kidney.

Structure of the Kidney.—The kidney is a compound tubular gland which exhibits many peculiarities, both in the anatomical features and distribution of the tubules themselves and in the arrangement of its vascular supply. The whole organ is invested with a fibrous *capsule*, continuous at the *hilum* with the connective tissue sheath of the blood-vessels and duct. The portion of the duct or *ureter* immediate to the kidney is considerably expanded, and is called the *pelvis of the ureter*. The small, well-marked concavity in the kidney at the hilum is termed the *sinus*, and its margin coincides with that of the expanded pelvis. If the kidney be laid open by a longitudinal section passing through the concavity at the hilum and the convexity of the general surface of the gland, it will be seen to consist of a series of more or less wedge-shaped lobules, the bases of which are directed to the circumference of the organ, while the apices project into the pelvis of the ureter. The pelvis is lodged in the sinus of the kidney, and when the latter is cut open, as above, may be seen to divide into two or three—more usually two—*infundibula*, which become moulded upon the projecting papillæ or apices of the wedge-shaped lobules, and the cup-shaped hollows thus receiving the papillæ are termed the *calyces of the pelvis*. They are about twelve in number in the human subject.

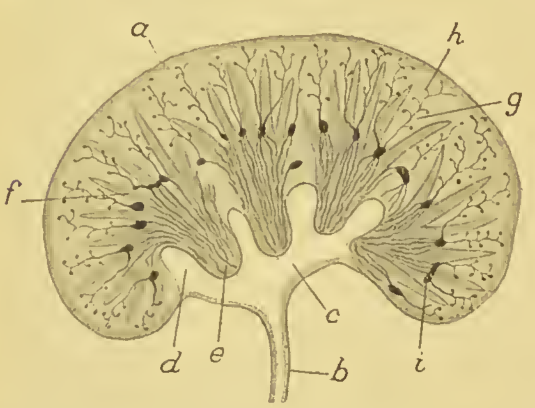

Fig. 268.—Diagrammatic representation of Parts of Kidney.

a, Capsule of kidney ; *b*, ureter ; *c*, sinus of kidney ; *d*, hollow between calyces which receives the papillæ of the Malpighian pyramids, *e* ; *f*, pyramid of Ferrein ; *g*, cortical labyrinth between pyramids of Ferrein ; *h*, interlobular vessel with branches going to glomeruli ; *i*, vascular arcade at junction of medulla and cortex.

The embryonic kidney consists of a number of lobes or lobules, each of which exhibits a medullary portion covered at its base, and to some extent at the sides, with cortex. The adjacent bases of the lobules are fused together, but as the surface of the organ dips distinctly at the lines of fusion, the lobulation is quite obvious to the naked eye. Such a lobulated state is very marked and

is permanent in the kidney of the ox and some other animals; but in man, as the organ undergoes development a more complete fusion occurs, the surface division into lobules entirely disappearing, and the cortex of the individual lobules assuming a more peripheral position as far as the kidney as a whole is concerned.

To return to the adult organ, its substance may be divided into *cortex* and *medulla.* The cortex is of a deep red colour and granular in appearance to the naked eye. It is narrower than the medulla, and represents the fused cortices at the bases of the original lobules. The medulla, on the other hand, is represented by the narrower ends of the wedges, and these ends are entirely free from each other where they project into the calyces. Further out the constituent portions of the medulla lie side by side, but separated by the presence of large vascular branches with their accompanying connective tissue, and by the *columns of Bertini*, which are prolongations between them of cortical substance—the remains of the lateral cortical covering of the original lobules.

The medulla differs somewhat from the cortex in appearance, as it is lighter in colour, and the wedges, sometimes called the *pyramids of Malpighi*, are not granular but striated. The portion of the medulla next to the cortex is usually distinguished from the rest as the *boundary layer*, and we thus have three zonal regions—cortical, boundary, and papillary. The zones vary in breadth in different species, but the medulla is broader than the cortex, and the boundary layer of the medulla is broader than the papillary part. Breadth is here used as synonymous with depth, *i.e.*, from the surface to the sinus. With the aid of a lens, radiating bundles may be made out passing from the bases of the Malpighian pyramids into the cortex. They are continuations of the medullary tubules or ducts, and the bundles will be seen to decrease in thickness as they approach the periphery of the cortex and cease in a pointed manner at a little distance from the capsule. Each Malpighian pyramid sends forth from its base several of these bundles, and they are known as the *medullary rays* or *pyramids of Ferrein.*

The cortex between the medullary rays is termed the *interpyramidal cortex*, and is distinctly granular in character, and dotted over with the *Malpighian corpuscles*—small round bodies, the nature of which we shall see presently. Speaking roughly, the interpyramidal cortex is the secretory, while the medullary rays and the pyramids of Malpighi represent the conducting portion of the gland.

The **connective tissue** of the kidney may almost be said to be conspicuous from its absence, as it is so small in amount. There is, however, a distinct capsule which normally separates readily from the cortical substance, as it is only united to it by continuations of the very delicate connective tissue between the tubules. In disease, however, such as chronic cirrhosis, this tissue may be greatly increased in amount, and the capsule may then become firmly bound to the organ and, as the expression goes, "will not peel." The connective tissue of the capsule and of the expanded end of the ureter enters the sinus, and is continued into the substance of the kidney, between the pyramids of Malpighi, where it supports the large vessels and becomes continuous with the very small amount between the tubules. There is a little more connective tissue between the tubules in the papillary region than elsewhere, and the basement membrane of the tubules is fused with it. In other parts the basement membrane appears as a more definite structure, and is readily distinguishable in section as a clearly-marked line with nuclei interspersed in it. It consists of a surface condensation of the scanty intertubular connective tissue.

The **tubules and vascular supply of the kidney.**—The *tubuli uriniferi*, or urinary tubules, are characterised by their unusual length, by the variations in the character of the epithelium lining them, by their dispositions (for the various sub-divisions of the tubules are not placed at haphazard but in definite parts of the cortex and medulla), and by the unbranched condition of the secretory portion. Their terminal ends are found in the cortex between the pyramids of Ferrein, and are expanded and lined by flattened epithelial cells. Perhaps we should say that in the earlier stages of development the end is expanded, for this expansion becomes invaginated by a tuft of capillary vessels, known as a *glomerulus*. The invagination is so complete that the glomerulus is entirely invested by the end of the tube, except around

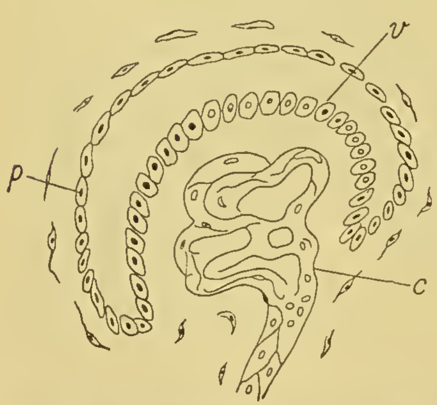

Fig. 269.—Development of Glomerulus of Kidney and Malpighian Capsule.

c, Capillary; *v*, visceral, and *p*, parietal layer of capsule.

its stalk, which is formed of the afferent and efferent vessels passing to it, and between which it forms the capillary connection. The invaginated cup thus formed will necessarily exhibit two layers, of which the outer (p) rests upon a basement membrane continuous with that of the rest of the tubule, and is composed of simple squamous nucleated cells; the epithelium and basement membrane together constituting the *Malpighian* or *Bowman's capsule.* The inner layer (v) of the cup consists of flattened cells, continuous with those of the outer layer around the stalk of the glomerulus, and closely applied to the capillary tuft without the intervention of a basement membrane, so that it cannot be distinguished as a separate structure, though the nuclei of the cells can be readily made out. Between the two layers of the cup a distinct space is left, which varies in size with the degree of distension of the capillaries of the tuft, and is continuous with the lumen of the uriniferous tubule, of which it forms the terminal part. The accompanying figure is a diagrammatic representation of one of the tubules we are describing, and at a is shown the cup which surrounds the glomerular tuft of capillary vessels. The Malpighian capsule is connected by a narrow and badly-defined neck with the *first convoluted tubule* (b), distinguished by its contorted or twisted character, which is considerably more marked than is expressed in the figure. This portion of the uriniferous tubule is notable for its breadth and the "secretory" character of its cells, which are large and roughly cubical, with an inner irregular or somewhat conical end projecting into the lumen. The latter varies in size, sometimes well marked, but not infrequently merely a stellate fissure in the midst of the granular cells, which

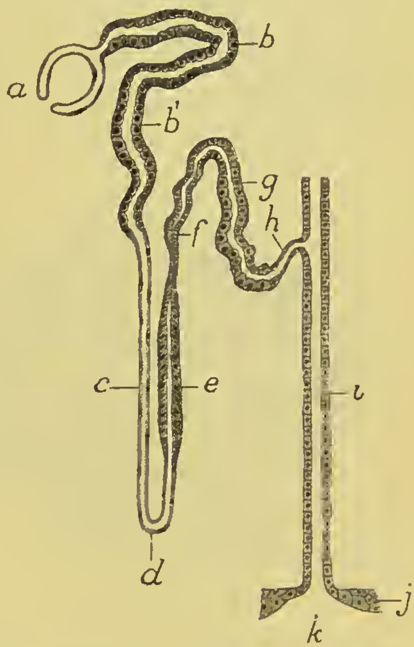

Fig. 270.—DIAGRAMMATIC REPRESENTATION OF A TUBULE OF THE KIDNEY, FROM ITS COMMENCEMENT ROUND A GLOMERULUS, TO ITS TERMINATION IN THE PELVIS.

a, Cup surrounding glomerulus; b, first convoluted tubule; b', spiral tubule; c, descending limb of Henle; d, loop of Henle; e, broad ascending limb of Henle; f, irregular tubule; g, second convoluted tubule; h, junctional tubule; i, straight collecting and discharging tubules; j, epithelium of pelvis; k, sinus of kidney.

possess a centrally placed nucleus, and are striated or "rodded" in their outer part.

The first convoluted portion continues as the *spiral tubule* (Fig. 270, *b′*) and exhibits much the same structure, but is straight rather than convoluted, except for the spiral twist which has given it its name; moreover, it is found not in the interpyramidal cortex, but in one of Ferrein's pyramids or medullary rays. The epithelium is a little lower than that of the first convoluted tubule and the lumen proportionately larger, nor are the cells so distinctly rodded in their outer part. At the junction of the medullary ray with the medulla the spiral tubule ends in the *descending limb of Henle's tubule* (Fig. 270, *c*), which, following the same course, traverses the boundary zone and passes into the papillary region for a varying distance. As will be seen in the diagram, this part of the tubule is characterised by its narrowness, and consists of a layer of flattened cells supported by a distinct basement membrane. The cells are clear, not granular, and each one of them is bulged in the centre to accommodate the nucleus. The outer contour of the tubule is straight, but the lumen is sinuous, because the cells are so arranged that the projections inwards of the nucleated centres are not opposite but alternate with each other. The epithelium, here, therefore, we see, is of the conducting variety, rather than granular or secretory, but the significance of this interposition of a conducting portion in this part of the tube is unknown to us. It corresponds apparently to the second conducting ciliated portion of the amphibian tubule, as seen in the frog and newt, the purpose of which we do not as yet understand.

Fig. 271.—SECTION OF KIDNEY, HUMAN (CORTEX).

a, Section of convoluted tubule; *b*, glomerulus; *c*, capillary vessel between tubules; *d*, intertubular connective tissue; *f*, capsule of Bowman.

After passing for a short distance into the papillary region, the tubule bends upon itself—the bend being known as *Henle's loop* (Fig. 270, *d*)—and passes backwards through the boundary layer as the *ascending limb of Henle's tubule* (Fig. 270, *e*). In the papillary region it retains the structure already described; but

this changes in the boundary layer, where the tubule is now broader, though still narrower than the convoluted portion, and the cells lining it are columnar in shape, with round or oval nuclei, deeply stained by reagents, striated in their outer part, and frequently arranged in a more or less imbricate manner; that is, they are not placed vertically on the basement membrane but with a slant in one direction. This broad part of the ascending limb of Henle, the cells of which present many of the characters of secretory epithelium, is a marked feature in the kidney of the dog. After traversing the boundary layer the ascending limb of Henle passes into the medullary ray, which it leaves as the *irregular tubule* (Fig. 270, *f*), to enter the interpyramidal cortex and lie amongst the convoluted tubules. The irregular tubule differs little from the broad part of Henle's ascending limb, but its outer contour presents sharp angles, and it follows a somewhat zigzag course. Its lumen, like that of the broad ascending limb, is small and regular, as contrasted with the sinuous lumen of the descending limb and Henle's loop. The irregular tubule is well marked in the dog. The *second convoluted* tubule (Fig. 270, *g*) follows the irregular one, and in structure resembles the first convoluted, and, like it, lies in the interpyramidal cortex. It terminates in the short junctional tubule (Fig. 270, *h*), which

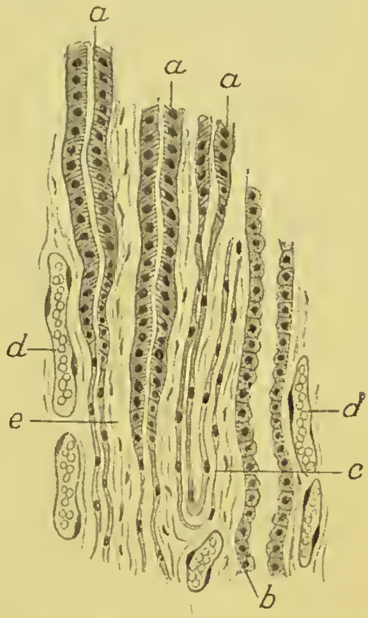

Fig. 272.—Longitudinal Section of Boundary Layer, Kidney of Dog.

a, Broad ascending limb of Henle's tube; *b*, straight collecting tubule; *c*, Henle's loop; *d*, capillary blood-vessels; *e*, connective tissue.

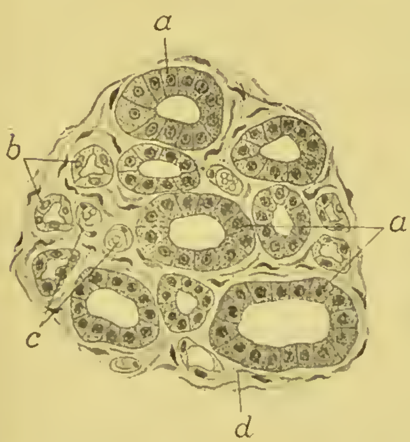

Fig. 273.—Transverse Section of Papillary Region, Human Kidney.

a, Transverse section of collecting tubes; *b*, transverse section of Henle's loop; *c*, capillary blood-vessels; *d*, connective tissue.

is lined by low cubical cells, and enters the adjacent medullary ray to open into a *straight collecting tube* (Fig. 270, *i*), which is lined by clear, nucleated, cubical cells and exhibits a wide lumen. After passing downwards through the boundary layer, several of

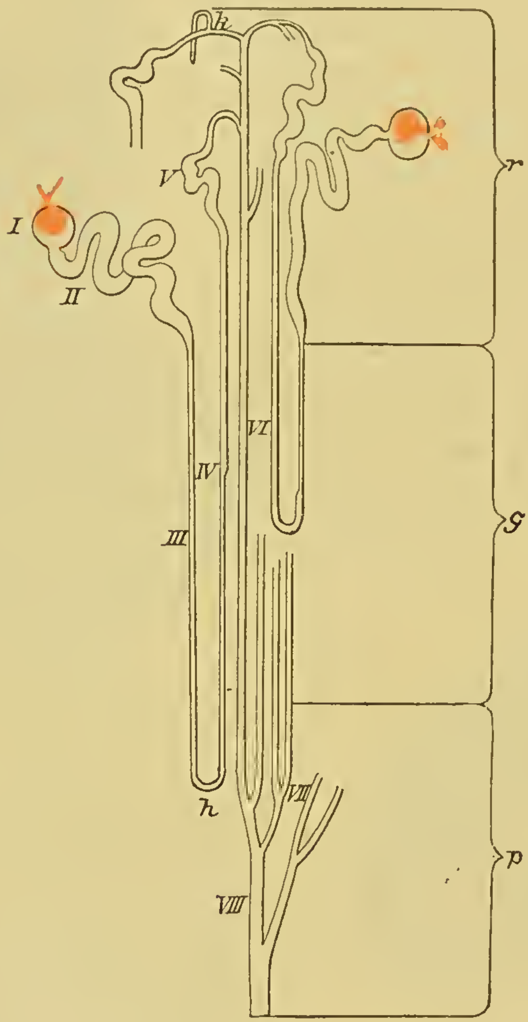

Fig. 274.—Diagrammatic representation of Kidney Tubules.
(After Ludwig.)

I, Bowman's capsule; *II*, first convoluted tubule; *III*, *IV*, descending and ascending limbs of Henle's tubule; *V*, second convoluted tubule; *VI*, straight collecting tubule; *VII*, other straight collecting tubules; *VIII*, discharging tubule; *h*, Henle's loop; *k*, junctional tubule; *r*, cortex; *g*, boundary layer; *p*, papillary region.

these unite in the papillary region to constitute a *large discharging tube*, or *tube of Bellini*, of which some twelve or twenty open into the pelvis about the apex of each papilla. These tubes are naturally larger than those which contribute to form them, present a conspicuous lumen, and the cells lining them are columnar rather than cubical; but otherwise they resemble them in structure. The epithelium lining them becomes continuous with the transitional epithelium of the pelvis reflected over the apices of the Malpighian pyramids.

The various parts of the tubules and the zones of the kidney in which they lie are again shown diagrammatically in Fig. 274.

The following table shows at a glance the position of the parts of the uriniferous tubule described :—

Cortex.	Interpyramidal cortex	Malpighian capsule. First and second convoluted tubules. Irregular tubule. Junctional tubule.
	Medullary ray or pyramid of Ferrein.................	Straight collecting tubule. Continuation of ascending limb of Henle. Spiral tubule.
Medulla.	Boundary zone	Straight collecting tubule. Descending limb of Henle. Ascending limb of Henle.
	Papillary region..............	Straight collecting tubule. Discharging tubule. Henle's loop.

The character of the uriniferous tubules is thus much less simple than that of the tubules of such a gland as the pancreas, and we shall see that this complexity is related to the difference in function of the different parts. At present it will be sufficient to note in passing that the cells of the first and second convoluted tubules, of the broad limb of Henle, and of the irregular tubule, have the characters we are wont to associate with secretion in the ordinary sense of the word; while the structure of the straight collecting and discharging tubes suggests for them the more passive duty of conducting the secretion to the surface upon which it is discharged. The junctional tubule evidently corresponds to the intermediate ductule of the salivary glands, while the descending limb of Henle, with its continuation as Henle's loop, appears to have no analogue in the glands we have previously considered, but corresponds with the second ciliated conducting portion of the uriniferous tubule of the frog. The epithelium of

Fig. 275.—Diagrammatic representation of the Blood-vessels of Kidney. (After Ludwig.) Arteries red; veins blue.

the expanded end of the tube covering a glomerular capillary tuft, though flattened, we shall find, plays a distinct part in the secretion of the urine, and its peculiar relation to the vascular supply of the kidney must be kept in mind. To the consideration of that vascular supply we may now turn.

The blood-vessels of the kidney.—The distribution of the blood-vessels in the kidney is as peculiar to it as the character and arrangement of the tubules. The branches of the renal artery pass outside the epithelium of the pelvis and plunge into the parenchyma of the organ between the pyramids of Malpighi. Passing radially outwards they form *arterial arcades* or *arches* at the outer margin of the medulla, and the arcades anastomose with each other. From the convexity of the vascular arches spring the *radiating* or *interlobular arteries* which lie in the interpyramidal cortex, midway between the pyramids of Ferrein. The interlobular arteries give off short *afferent arterioles*, one to each glomerulus, and in a vertical section of injected kidney under a low power we see the radiating interlobular vessel with a row of glomeruli on each side of it supplied with afferent branches, the glomeruli having some resemblance to berries, the afferent arterioles to their stalks, and the interlobular artery to the stem upon which these are set. The afferent arteriole enters the invaginated cup we have described, formed by the end of a urinary tubule, and breaks up into capillary vessels, forming the glomerular tuft, the blood being received from them by an *efferent vessel* which leaves the glomerulus at the point where the artery enters it. After leaving the glomerulus the short efferent vessel breaks up into a capillary network between the

tubules of the cortex, both pyramidal and interpyramidal; and from this network the blood is conducted by *interlobular radiating veins*, which lie with the arteries in the interpyramidal cortex, to corresponding *venous arches*, and thence by branches passing downwards between the Malpighian pyramids and uniting to form the renal vein. The vascular arrangement, therefore, reminds us of the portal system of the liver, since the efferent vessel of the glomerulus, formed by the union of the glomerular capillaries, breaks up into a capillary network again.

We have yet to notice the blood-supply of the medulla, which is provided by the *arteriolæ rectæ* springing from the concave, lower or inner side of the arterial arches and passing radially to the apex of the Malpighian pyramids between the tubules, around which they give off a capillary network, the blood being returned by *venulæ rectæ*, which terminate in the venous arcades. The capillary networks of the cortex and medulla are continuous with each other. A few of the arteriolæ rectæ are continuations of the efferent vessel of the glomeruli near the medullary margin, but all the venulæ rectæ open into the venous arches.

There is a small but somewhat important anastomosis between the vessels at the periphery of the cortex and those of the capsule, and between these again and the vessels of the extra-peritoneal fat.

The nerves of the kidney are referred to later.

The Composition of Urine.

Normal urine is a clear yellowish fluid with a saline taste and acid reaction, its specific gravity being on an average 1020, or roughly from 1015 to 1025; but this is affected necessarily by the amount of water taken. The average quantity excreted in twenty-four hours is from 40 to 50 ounces, or from 1200 to 1500 c.c.; but, like the specific gravity, this will be influenced by the amount of fluid imbibed, and also, too, by the state of activity of the skin. Other things being equal, the more water that is given off by the skin, as when the sweat glands are secreting freely, the less will pass by the kidneys; whereas if the skin is comparatively inactive, as in winter, the kidneys excrete more to make up the deficiency. That is to say, the skin and kidney are complementary to each other so far as the excretion of water is concerned.

The constituents of urine will not all have the same history. Thus some of them have been simply absorbed from the alimentary canal in the form in which they entered it, and are

excreted by the kidney unchanged; others are the products of changes which are comparatively superficial and have taken place in the alimentary canal or in the blood-stream; while yet others have resulted from the deeper tissue metabolism. It consists mainly of water, inorganic salts, and its chief constituent urea; but there are also found other nitrogenous derivatives in small amount, such as uric acid, xanthin, hypoxanthin, hippuric acid and kreatinin; urea, and at least some of the others resulting from proteid metabolism in the tissues. There are also other organic bodies in very small quantities, united with sulphuric acid and derived from putrefaction of proteids in the alimentary canal, such as K-phenyl sulphate, K-indoxyl sulphate, and K-skatol sulphate.

The average composition of human urine is shown in the following table, but allowance must be made for great variations, according to the nature of the food and other conditions:—

Amounts of the several urinary constituents passed in twenty-four hours (Parkes)—

	By an Average Man of 66 Kilos.		Per Kilo of body weight.
Water		1500·000 grms.	23·0000 grms.
Total Solids			1·1000
Urea	33·180		·5000
Uric Acid	·555		·0084
Hippuric Acid	·400		·0060
Kreatinin	·910		·0140
Pigment, &c.	10·000		·1510
Sulphuric Acid	2·012		·0305
Phosphoric Acid	3·164		·0480
Chlorine	7·000 (8·21)		·1260
Ammonia	·770		
Potassium	2·500		
Sodium	11·090		
Calcium	·260		
Magnesium	·207		
		72·000	

The **acidity of urine** is not caused by any free acid, but is due to the presence of acid sodium phosphate. The degree of acidity varies inversely with the acid secreted by the stomach, being decreased during gastric digestion and increased again when this is over. The diet also influences it. A vegetable diet, owing to the excess of alkalies present, diminishes it; indeed, in herbivora we find the urine normally alkaline, while in carnivora it is normally acid, as it is also in fasting herbivora, which are virtually living on their own tissues.

After discharge, the acidity of the normal human urine at first increases, owing to what is known as the *acid fermentation* resulting in the formation of lactic and acetic acid by decomposition of the pigment and the deposit of acid sodium urate in an amorphous form. Urates may be deposited in fresh urine on cooling alone, as they are more soluble in warm than cold water, but very frequently this does not take place until the acidity is increased by the acid fermentation. The uric acid set free is deposited in a crystalline form coloured by pigment, and crystals of calcium oxalate may also appear. Subsequently, if the urine be allowed to stand in a warm place under conditions favouring putrefaction, *alkaline fermentation* supervenes and it becomes strongly ammoniacal, owing to the action of ferments—the micrococcus and bacterium ureæ—which are conveyed to it by the air, and cause the urea to take up water and form ammonium carbonate, thus :—

$$\underset{\text{Urea.}}{N_2H_4CO} + \underset{\text{Water.}}{2H_2O} = \underset{\text{Carbonate of ammonium.}}{(NH_4)_2CO_3}$$

A deposit also occurs in this alkaline urine, and consists of *knife-rest* crystals of triple or ammonio-magnesic phosphate, formed by the union of ammonia with the magnesium phosphate normally present, of amorphous earthy phosphates, and of spinous balls of acid ammonium urate. We may now pass to the consideration of the more important urinary constituents.

Nitrogenous crystalline substances.—Of these the most important is **urea**, the form in which the greater part of the nitrogen leaves the body, and the amount excreted may be taken as a measure of proteid katabolism. The normal percentage of urea in human urine is about two per cent., but this percentage will necessarily vary with the relative amount of water present. The excretion of urea is greatest about three hours after a meal, especially if it be rich in proteids, as the tissues are stimulated to increased activity. The urea excreted, however, is not derived from the food immediately taken, which has probably first to be assimilated and built up into the tissues. The increase of urea after a meal is due to increased discharge from the tissues to make way for the new proteid brought to them by the blood-stream.

Urea has the composition N_2H_4CO and is related to two groups of substances. In the first place, it is converted by hydration to ammonium carbonate, as we have just seen, and thus is related to the ammonia group. Secondly, it is isomeric with

ammonium cyanate, from which it may be obtained by heating, thus :—

$$\underset{\text{Amm. cyanate.}}{NH_4CNO} = \underset{\text{Urea.}}{N_2H_4CO}$$

and is thus related to the cyanogen group. This last equation is of especial interest, as the synthesis of urea, *e.g.*, from ammonium sulphate and potassium cyanate, was the first example of a complex product of living matter produced in the laboratory (Wöhler).

It occurs in urine to the extent of about 30 grms. daily, and may be obtained by evaporation of the urine to a syrup, followed by extraction with hot alcohol and evaporation. The crystals occur as four-sided prisms with oblique or pyramidal ends, as seen in Fig. 4, page 14. They are anhydrous and readily soluble in water or hot alcohol. On the addition of nitric or oxalic acids to a concentrated solution of urea, crystals of nitrate or oxalate of urea separate out (Figs. 5 and 6). When crystals of urea are heated in a test-tube it decomposes, ammonia being being given off and *biuret* left, thus :—

$$\underset{\text{Urea.}}{2N_2H_4CO} = \underset{\text{Biuret.}}{C_2O_2N_3H_5} + \underset{\text{Ammonia.}}{NH_3}$$

If the residue be dissolved in water and treated with a trace of copper sulphate and excess of alkaline hydrate, a rose-pink colour results (*cf.* Biuret reaction for albumoses and peptones, page 3).

We have seen that under the influence of micro-organisms, urea splits up into carbon dioxide and ammonia, and this may also be accomplished by heating a watery solution of urea in a sealed tube. Nitrous acid carries the decomposition further, water, nitrogen and carbon dioxide resulting, thus :—

$$\underset{\text{Urea.}}{N_2H_4CO} + \underset{\substack{\text{Nitrous}\\\text{acid.}}}{2HNO_2} = \underset{\substack{\text{Carbon}\\\text{dioxide.}}}{CO_2} + \underset{\text{Water.}}{3H_2O} + \underset{\text{Nitrogen.}}{2N_2}$$

The same action by hypobromous acid forms the basis of the commonest quantitative test for urea in urine, thus :—

$$\underset{\text{Urea.}}{N_2H_4CO} + \underset{\substack{\text{Hypobromite}\\\text{of soda.}}}{3NaBrO} = \underset{\substack{\text{Carbon}\\\text{dioxide.}}}{CO_2} + \underset{\substack{\text{Bromide}\\\text{of sodium.}}}{3NaBr} + \underset{\text{Water.}}{2H_2O} + \underset{\text{Nitrogen.}}{N_2}$$

Quantitative estimation of urea.—It is important that we should be in possession of an easily workable method of estimating the amount of urea in urine daily from the clinical point of

view, as it varies considerably in disease. In acute febrile conditions it is increased in amount up to the crisis, after which it falls to normal or subnormal when the fever is over. When the tubules of the kidney are involved in tubular nephritis, the amount excreted may be greatly decreased, but this must be distinguished from decrease in production. In chronic interstitial disease of the kidney, in which the connective tissue is affected, no diminution may occur.

The most generally serviceable method of estimating the amount of urea is founded on the liberation of nitrogen by the action of hypobromite of soda, as shown in the above equation. The carbon dioxide set free is absorbed by an excess of sodium hydrate, and the nitrogen is collected over water in a measuring tube specially designed for the purpose, or in an inverted burette, which serves the purpose equally well. The nitrogen thus is the only gas which comes off, and the amount of it is taken as a measure of the urea present in the sample of urine tested—·1 grm. of urea giving off 35·4 c.c. of N at 0°C. and 760 mm. pressure. The apparatus employed in this — the *hypobromite method*—consists of a bottle connected by india-rubber tubing with a measuring tube, which is held by a clamp within a cylindrical jar containing water, and can be lowered or raised at will. The hypobromite solution may be made by mixing 100 grms. of NaHO with 250 c.c. of water and adding to the solution 25 c.c. of bromine. As it is of advantage to have the hypobromite freshly made, it is, however, preferable to make it in smaller quantity unless a number of tests are to be performed. Twenty-five c.c. of the hypobromite are measured and poured into the bottle. Of the urine to be examined 5 c.c. are measured into a small tube provided for the purpose, and the tube is lowered into the bottle, care being taken that none of the urine is spilt in doing so. The india-rubber stopper of the bottle, through which the glass tube passes, is then firmly fixed in position. The rubber tube is connected with the burette by a glass T-piece, the upper limb of which is connected with a short piece of rubber tubing, which may be closed by a pinch-cock. With this tube open the measuring tube is lowered till the zero mark corresponds with the surface of the water in the cylindrical jar. The tube is then closed and the whole apparatus should be found air tight.

The bottle containing the hypobromite is now gradually tilted so as to allow the urine to run out from the small tube and mingle with the hypobromite solution. The mixing of the fluids results in a brisk evolution of gas and the development of a considerable

amount of heat; so that it is well to immerse the bottle in water of the same temperature as that of the water in the cylinder, so as to assist the cooling and so reduce the time which has to elapse before the result can be read off. As the gas is evolved it passes up the india-rubber tube and enters the measuring tube, in which the water correspondingly sinks. In a few minutes (when the apparatus is cool) the measuring tube is raised till the water inside it is again level with that outside, and the amount of gas read off in c.c. Now we have seen that 35·4 c.c. of N represent ·1 grm. of urea. To take the simplest case then, if 35·4 c.c. are read off the measuring tube, the 5 c.c. of urine tested contains ·1 grm. of urea. If the 5 c.c. was a sample of the mixed urine of twenty-four hours, and the total quantity of this was 1500 c.c., the amount of urea excreted would be 30 grms.,

$$\text{for } \tfrac{1500}{5} \times \cdot 1 = 30 \cdot 0.$$

If more or less than 35·4 c.c. are read off, a simple sum in proportion gives the amount in urea in the 5 c.c. to which it will correspond. The measuring tubes in some forms of the apparatus are graduated in percentages of urea. It does not, however, matter much what particular form of apparatus is employed so long as the operator is accustomed to work with it and understands it. Care should be taken that it is air-tight when the test is made, and that the readings are taken at the same temperature and pressure, *i.e.*, that the apparatus has had time to cool before the second reading is taken, and that the water inside and outside the measuring tube is at the same level.

Another method of estimating the amount of urea is that devised by Liebig. Here 40 c.c. of urine are mixed with 20 c.c. of baryta mixture, which precipitates the sulphuric and phosphoric acids. Of the filtrate 15 c.c. (corresponding to 10 c.c. of urine) are placed in a beaker and a solution of mercuric nitrate run into it from a burette. This *standard solution* of mercury is of such a strength that 1 c.c. of it will combine with ·01 grm. of urea. The solution is allowed to run in by small instalments, so that the exact moment when a precipitate ceases to form and there is *free* mercuric nitrate in the mixture may be ascertained. This is determined by testing the mixture from time to time with drops of sodium carbonate on a white slab. The sodium carbonate, or *indicator* as it is called, gives a yellow colour as soon as there is free mercuric nitrate present. As each c.c. of the standard solution corresponds to ·01 grms. of urea, ·01 multiplied by the number of c.c. used will give us the amount of urea in the 10 c.c. of urine tested, and from this the percentage is easily

calculated. Both these methods are satisfactory in the hands of those accustomed to them, but the first is perhaps the simplest to work with.

Uric acid in mammals accounts for a very small quantity of the total nitrogen excreted, but in the semi-solid urine of birds and reptiles it replaces urea as the chief nitrogenous waste product. It is a weak dibasic acid, with the composition $C_5N_4H_4O_3$, and occurs in urine combined with bases to form salts, but not as a free acid. Crystals of uric acid may be obtained by acidulating human urine with hydrochloric acid and allowing to stand for a day or so, when they are deposited on the sides of the glass and look like grains of cayenne pepper, as they are coloured by the pigment of the urine. They belong to the rhombic system, and are sometimes whetstone-shaped, sometimes barrel-shaped, or arranged in the form of rosettes or wheat sheaves (Figs. 276 and 277). Uric acid is almost insoluble in water (1 in 15,000 parts of cold water), in this way contrasting with urea, and it is also insoluble in alcohol and ether. It has been synthetically produced from glycin and urea.

Fig. 276.—Uric Acid Crystals.

Uric acid occurs in urine in solution as the acid urates of sodium and potassium, and to a less extent combined with ammonium and calcium. Acid sodium urate forms the greater part of the "brick-dust" ("lateritious") deposit which often occurs as the urine cools or after the onset of acid fermentation, while ammonium urate is deposited when it has become ammoniacal. Urates are found also forming urinary calculi and gouty deposits. In gout the excretion of uric acid may be diminished to one-ninth of the normal, and it accumulates in the blood and tissues, forming concretions of sodium urate in various situations. The amount of uric acid excreted is increased after a meal

especially if it contains nucleo-proteids in abundance, *e.g.*, thymus gland of calf.

Preparation of uric acid.—Uric acid may be prepared from serpent's urine by dissolving it in dilute sodium hydrate and precipitating the filtrate, which contains neutral sodium urate, with a current of carbon dioxide to throw down the acid salt. If the precipitate be boiled with dilute hydrochloric acid, colourless crystals of uric acid deposit on cooling.

Qualitative test for uric acid.—The murexide test is so called because of the resemblance of the colour produced to the purple derived from certain snails (murex). Some of the uric acid or urate is heated with a little dilute nitric acid in a porcelain capsule, a yellowish-red residue being left, which becomes purple-red (murexide) on the addition of ammonia, due to the formation of ammonium furfurate. Potassium and sodium hydrates produce a violet colour.

Fig. 277.—Uric Acid Crystals.

Quantitative estimation of uric acid.—Five c.c. of pure hydrochloric acid are added to 100 c.c. of urine, and the mixture allowed to stand for forty-eight hours. The crystals are collected on a small weighed filter, washed in as little water as need be, dried and weighed. This method is not quite satisfactory as it gives too small a result. A better one is that of Hopkins, in which the urine is saturated with ammonium chloride and all the uric acid precipitated as ammonium urate. In two hours' time the precipitate is collected on a filter and washed with saturated solution of ammonium chloride. It is then dissolved in weak alkali, and the uric acid precipitated from the solution by hydrochloric. The crystals are collected on a weighed filter, dried and weighed.

There are other methods—Salkowski's, modified by Ludwig and Haycraft, Whitney's modification of Hopkins' method, &c.—for which the student is referred to larger works.

The **xanthin** group of substances is nearly related to uric acid, and includes xanthin, hypoxanthin, guanin, &c. Xanthin has the formula $C_5H_4N_4O_2$, thus containing one atom of oxygen less than uric acid, and being intermediate between it and hypoxanthin or sarkin, $C_5H_4N_4O$, which is found in the urine of leukæmic patients. The substances of the xanthin group occur in very small amount in normal urine, but, like uric acid, are increased by a diet of nucleo-proteid.

Hippuric acid occurs only to a small extent in the urine of man, but in abundance in that of herbivora. It has the formula $C_9H_9NO_3$, and is formed in the body from the union of benzoic acid and glycin, thus:—

$$\underset{\text{Benzoic acid.}}{C_7H_6O_2} + \underset{\text{Glycin.}}{C_2H_5NO_2} = \underset{\text{Hippuric acid.}}{C_9H_9NO_3} + \underset{\text{Water.}}{H_2O}$$

and to this we shall have to refer later. It is found, therefore, that food-stuffs containing benzoic acid, or substances belonging to the aromatic group, largely increase the amount of hippuric acid and account for its predominance in herbivora. As illustrating its direct relation to the food in these animals, it is stated that it is absent from the urine of sucking calves. The small quantity found in the urine of man may have the same origin, or may be derived from the metabolism of proteid matter containing an aromatic constituent. Like uric acid, it does not occur free, but united with bases to form hippurates.

Fig. 278.—Hippuric Acid Crystals.

Hippuric acid may be prepared from horse's or cow's urine by concentrating and acidulating with pure hydrochloric acid. The precipitate is washed in cold water, dissolved in hot water, the solution filtered, and from the filtrate crystals of hippuric acid separate on cooling as colourless four-sided prisms with pyramidal

ends. When the dry crystals are heated in a test-tube the hippuric acid is decomposed, benzoic acid and ammonium benzoate condensing in the upper part of the tube, while oily drops of benzo-nitrile remain at the bottom.

Kreatinin has the formula $C_4H_7N_3O$, and differs from the kreatin of muscle in possessing one molecule of water less. It can be obtained from kreatin by boiling with dilute sulphuric acid, thus:—

$$\underset{\text{Kreatin.}}{C_4H_9N_3O_2} = \underset{\text{Kreatinin.}}{C_4H_7N_3O} + \underset{\text{Water.}}{H_2O}$$

It is a constant constituent of human urine, and is probably derived partly from the kreatin of muscle and partly from flesh food. It crystallises in the form of colourless oblique rhombic columns, and unites with various acids and salts, such as silver nitrate, mercuric chloride and zinc chloride, to form crystalline compounds. Kreatinin-zinc-chloride crystallises in the form of rosettes or groups of fine needles, and has the formula $C_4H_7N_3OZnCl_2$.

Weyl's test for kreatinin consists in the addition of a few drops of dilute sodium nitro-prusside to urine, followed by weak caustic soda, which results in the production of a ruby-red colouration turning to yellow. On adding acetic acid and heating, the colour changes to green and then to blue.

Non-azolised organic substances, such as oxalic, lactic, formic, butyric, acetic and succinic acids, are sometimes present in traces in normal urine. A small quantity of CO_2 gas can be extracted from urine which has not been exposed to the air, *i.e.*, which has been collected direct from the body.

Pigments of the urine.—Our knowledge of the urinary pigments is not very complete. One of the most important of these, **urobilin**, has a reddish colour, and appears to be an iron-free derivative of hæmoglobin. It is identical with the stercobilin of the fæces, which is derived from the bile pigment, some of the stercobilin being reabsorbed and excreted in the urine as urobilin. Urobilin has the formula $C_{32}H_{40}N_4O_7$, and may be obtained from urine by extracting with chloroform or ether and allowing the solution to evaporate. The pigment is present in increased quantity in certain febrile conditions, and a distinction has been made between normal and febrile urobilin, but it is doubtful if any such distinction really exists. According to some, urobilin does not exist in healthy unaltered urine as such,

but as a chromogen, which on exposure to the air undergoes oxidation, resulting in the production of the pigment proper. **Urochrome** is the chief colouring matter, and gives it its yellow colour. On exposure to air it becomes red through oxidation to **uroerythrin,** which gives to the deposit of urates its reddish or pink colour. Other pigments, such as *uro-hæmato-porphyrin*, *urinary melanin*, and *methæmoglobin*, occur only pathologically, and are not found in normal urine.

Ferments.—Urine usually contains traces of amylolytic and proteolytic ferments, which vary in amount during the twenty-four hours according to meals. Their presence is probably due to absorption from the glands of the alimentary canal into the blood-stream and subsequent excretion by the kidney.

Inorganic constituents of the urine.—These consist chiefly of chlorides, phosphates, sulphates and carbonates, the bases being sodium, potassium, calcium, magnesium and ammonium. Some of the salts, *e.g.*, the chlorides and most of the phosphates, are taken into the body as food and excreted in the form in which they enter it. Others, again, such as some of the phosphates and most of the sulphates, are the result of oxidation of the phosphorus and sulphur of proteids, and are thus the outcome of metabolism. As we have seen, the nitrogen of proteid waste leaves the body as urea and uric acid, and we may now say that the sulphur leaves it as the sulphuric acid of the sulphates of urine; and the excretion of urea and sulphates proceeds proportionately. Of the inorganic constituents, sodium chloride is the most abundant, the amount excreted daily averaging 12 grms.

Chlorides.—The chief of these is **sodium chloride,** a much smaller amount of the chlorine being united with potassium. The chlorides are almost entirely derived from the chlorides of the food, sodium chloride itself being excreted by the kidney unchanged. Some of the sodium chloride of the blood undergoes decomposition to provide the hydrochloric acid of the gastric juice. In diseases accompanied by effusions, such as pneumonia and dropsies, the amount of the salt in the urine is greatly diminished, as it is also in prolonged diarrhœa and profuse sweating. Chlorides are tested for qualitatively by the addition of a few drops of nitric acid to the urine to keep the phosphates in solution, followed by nitrate of silver solution, when a white curdy precipitate of chloride of silver, soluble in ammonia, is thrown down.

Phosphates.—The phosphoric acid of the urine is present in the form of **acid sodium phosphates** (NaH_2PO_4) and the di-hydrogen **phosphates of calcium** and **magnesium**—$Ca(H_2PO_4)_2$ and $Mg.(H_2PO_4)_2$. They are largely derived from the alkaline and earthy phosphates of the food, partly from the metabolism of proteids rich in phosphorus, *e.g.*, nuclein, and partly from complex fats containing phosphorus, such as lecithin. On the addition of an alkali, the earthy phosphates of calcium and magnesium are converted to the basic salts, and these being insoluble are precipitated, the sodium phosphate remaining in solution. The earthy phosphates are also precipitated, as we have seen, in the alkaline fermentation of urine, when calcium phosphate in the form of stellar clusters of prisms and coffin-lid crystals of triple or ammonio-magnesic phosphate are deposited as the result of the action of the ammonia set free by the decomposition of urea (Fig. 279). The triple phosphate may also crystallise in the form of feathery stars, as it is particularly liable to do when thrown down artificially (Fig. 280). Normal urine gives no precipitate on heating; but in some pathological urines the earthy phosphates are precipitated

Fig. 279.—Triple Phosphates (Coffin-lid Type).

Fig. 280.—Triple Phosphates (Stellar Type).

in an amorphous form on boiling, owing to the CO_2 which kept them in solution being driven off. Such a precipitate of phosphates is readily distinguishable from albumen from its solubility in acids.

Qualitative tests for phosphates.—(1) If ammonia be added to urine there is a precipitate of earthy phosphates, the alkaline phosphates remaining in solution. If the filtrate be treated with magnesia mixture, the alkaline phosphates are thrown down as ammonio-magnesic or triple phosphate. (2) If the urine be mixed with its own quantity of nitric acid, and a little ammonium molybdate be added, then on heating, a yellow precipitate of ammonium phospho-molybdate reveals the presence of phosphoric acid.

Quantitative estimation of phosphoric acid.—The amount of phosphoric acid present in urine may be estimated by a volumetric method comparable to that of Liebig for urea. Here the standard solution is one of uranium acetate, which combines with phosphoric acid in definite proportions. As soon as *free* uranium acetate occurs in the urine being tested, its presence is revealed by the indicator, potassium ferrocyanide, with which it gives a brown colour, due to the formation of uranium ferrocyanide.

Sulphates.—The sulphates of urine are derived mostly from the oxidation of the sulphur of proteids, *i.e.*, from metabolic changes, and to a small extent only from sulphates taken in the food, the **sulphuric acid** being combined for the most part with **potash** and **soda**. About one-tenth, however, of the total amount of the acid excreted is found in the *ethereal sulphates* of the urine, to which reference has already been made. These substances, though many of them do not contain nitrogen, are derived from bodies of the aromatic series, resulting from the action of micro-organisms on proteids in the alimentary canal. They are thus putrefactive products, and their amount in the urine is largely proportional to the putrefactive changes taking place in the intestine. Thus they are found to be increased in quantity in cholera, typhus, carcinoma of the stomach, peritonitis—in those diseases, in fact, which favour the action of the micro-organisms concerned. The ethereal sulphates include *potassium-phenyl-sulphate* ($C_6H_5KSO_4$), *potassium-skatoxyl-sulphate* ($C_9H_8NKSO_4$), and *potassium-indoxyl-sulphate* ($C_8H_6KNSO_4$). The latter substance forms indigo-blue on oxidation, and is known as the *indican* of the urine. *Sulphate of pyro-catechin* is also sometimes present in small quantity.

The inorganic sulphuric acid may be tested for qualitatively by acidulating the urine with hydrochloric acid to prevent the precipitation of phosphates, and adding a few drops of barium chloride, when a white precipitate of sulphate of barium is thrown down. It may be estimated quantitatively by acidulating with acetic acid, precipitating with barium chloride, and weighing the dried and incinerated precipitate of barium sulphate. One grm. of barium sulphate corresponds to ·41 grms. of sulphuric acid.

Carbonates only occur in alkaline urine, and thus are found in the urine of herbivora and vegetarians. They are derived from the carbonates and vegetable acids (malic, citric, and tartaric) of the food.

The **deposits** which may occur in urine, both normal and pathological, are of so much importance that we may review them shortly here.

Urinary deposits may be composed of formed structural elements, such as blood-corpuscles, pus, and epithelial cells, or of chemical substances, such as phosphates and urates, or of a mixture of the two. The chemical deposits are those with which we are now concerned.

Urine, as we have seen, is normally acid in reaction in man and the carnivora, and alkaline in the herbivora, but it may be alkaline even in man upon a diet rich in vegetables. Urine, however, which issues from the ureters with an acid reaction may become alkaline in the bladder, due to fermentation changes within the viscus; and all urine after suitable exposure to the air undergoes the alkaline fermentation due to the activity of the micrococcus and bacterium ureæ. As we should anticipate, different chemical substances are found deposited in acid and alkaline urines respectively.

Deposits in acid urine.—Of these by far the commonest and most copious is the *uratic*, which may occur on cooling in perfectly normal urine if it be at all concentrated, and usually characterises the urine of fevers. Urates are often also deposited when the acid fermentation already referred to takes place, though previously held in solution, even on cooling. The deposit is composed of *acid sodium urate* and is pinkish-red in colour, due to the pigment uro-erythrin. It is amorphous under the microscope, to the naked eye giving somewhat the appearance of a layer of brick-dust. It rapidly dissolves on heating, and, apart from its colour, the deposit is readily recognised as uratic

by this test. In urine which has undergone the acid fermentation, *uric acid* may appear in a form resembling cayenne pepper to the naked eye, the crystals being pigmented, and whetstone-shaped, barrel-shaped, &c., under the microscope; and in such a urine, envelope or hour-glass forms of *calcium oxalate* may also be found. *Cystin* is found as a rare form of deposit in acid urine as six-sided colourless plates.

Deposits in alkaline urine.—The white *phosphatic* deposit found in alkaline urine consists of the *amorphous earthy phosphates, triple ammonio-magnesic phosphate* in the form of knife-rest crystals or feathery stars, and often spinous balls of *ammonium urate* (Fig. 281). The precipitate of phosphates is not dissolved on heating, and may even be increased by it, thus contrasting markedly with the urates. It may be distinguished from albumin in the urine by the fact that it dissolves on the addition of an acid, *e.g.*, acetic. *Calcium carbonate* is found more often as a deposit in the urine of herbivora than in that of man, and is readily recognisable as it dissolves with effervescence on the addition of acetic acid.

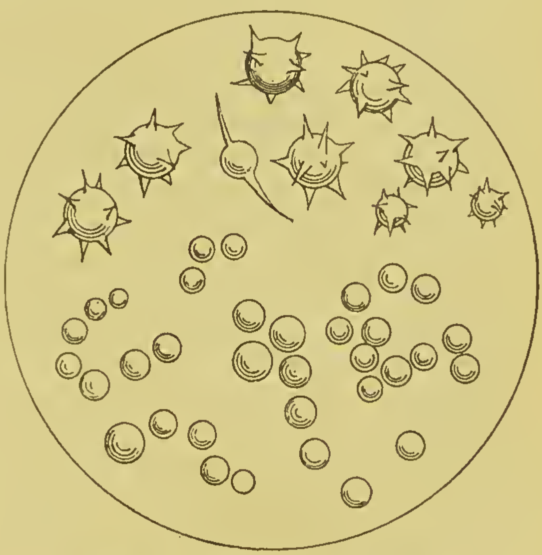

Fig. 281.—Ammonium Urates.

Leucin and tyrosin crystals are found rarely in urinary deposits.

Abnormal constituents of the urine.—The structural elements which, as already stated, may form deposits in urine, *e.g.*, blood- and pus-corpuscles and epithelial cells, are not found in normal urine but occur in disease, and with them must also be mentioned tube-casts—epithelial, fibrinous, or composed of blood—which are commonly present in affections of the kidney. In addition to these structural elements, certain chemical substances appear in the urine as abnormal constituents, and the most important of these are proteids, including serum-albumin and globulin, sugar in the form of dextrose, bile salts, and the pigments of blood and bile and their derivatives. Other substances, also, which are

not proper constituents of the food, are often excreted unchanged by the kidney and appear in the urine as abnormal constituents. The most important abnormal constituents clinically are *albumin*, which occurs in the albuminuria of kidney disease, and *sugar*, found in the glycosuria of diabetes mellitus.

Albumin in urine.—Serum-albumin and globulin occur most constantly in pathological urine as the result of kidney disease; but albumose and peptone may also be present, though much more rarely, as in cases of osteomalacia.

The test of *heat and nitric acid* is the most generally satisfactory one for detecting the presence of albumin in urine. Some of the urine is boiled in a test-tube and a few drops of nitric acid added. If albumin be present the application of heat separates the coagulable proteids, and the precipitate is either unaffected or increased by the addition of nitric acid. Phosphates are also sometimes precipitated from urine by heating, but their precipitate is dissolved on the addition of nitric acid. If the urine to be examined is found to be alkaline it should be acidulated before boiling, otherwise the albumin is not precipitated. Urine which is not "clear" should always be filtered before testing for albumin, as it is desirable to be able to recognise the faintest appearance of cloudiness on heating.

Heller's nitric acid test affords another means of detecting the presence of albumin. A little of the urine to be examined is poured carefully upon some nitric acid in a test-tube, when a zone of white at the junction of the fluids indicates the presence of albumin. If the patient be taking copaiba, however, the resin, under the action of the acid, will give rise to a slight milkiness in the same situation. A third qualitative test for albumin may be performed with *ferrocyanide of potassium and acetic acid.* The urine is acidulated with acetic acid and a few drops of ferrocyanide added, causing a white flocculent precipitate. Fourthly, albumin in urine is also precipitated by a saturated solution of picric acid, and, according to Dr Johnson, this affords the most delicate test for small quantities.

The quantitative estimation of *albumin* may be conveniently carried out by means of *Esbach's Albuminimeter*, a test-tube-like glass cylinder which is graduated in grms. of albumin per 1000 c.c. of urine, and marked at two levels with the letters U and R. The cylinder is filled with urine up to the mark U, and with the reagent (20 citric acid, 10 picric acid, and 970 water) up to the mark R. The tube is then closed with a cork and inverted two or three times in succession to ensure mixture of the fluids. It is then allowed to stand upright for twenty-four hours, and

the amount of albumin precipitated is then read off in grms. per 1000 c.c. (or litre) of urine. Thus if the upper level of the precipitate corresponds on the scale to the figure 4, then 4 grms. of albumin are found in 1000 c.c. of urine, *i.e.*, the percentage of albumin present is ·4. If the amount present is greater than this, it increases the accuracy of the method to dilute the urine with its own quantity of water before testing and correct the reading afterwards, *i.e.*, multiply the result by two. This method of estimating albumin has its disadvantages, but it affords a ready means of comparing the amounts of albumin in the urine from day to day.

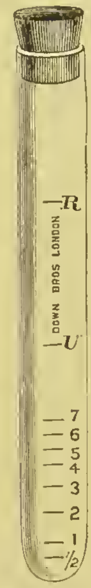

Fig. 282.—ESBACH'S ALBUMINIMETER.

The albumin may also be estimated by the *gravimetric method*, *i.e.*, it is precipitated, dried and weighed. The urine is first boiled, acetic acid being added as long as it causes any increase in the precipitate. The precipitate is then collected on a weighed filter, washed first with hot water and then with hot alcohol, and dried in an air bath at 110°C. It will be apparent at once that this is not a method suitable for the "busy practitioner," who will find Esbach's tube much more generally useful.

Sugar in urine.—This occurs in diabetes mellitus, a disease which is characterised by excessive appetite and thirst, general emaciation, and constitutional disturbance. The urine is increased in amount, its specific gravity is high, and sugar in the form of dextrose is present to the extent of 1 to 5 per cent., or it may be more. Temporary glycosuria may be produced by puncture of the lower part of the floor of the fourth ventricle in the region of the centre of the vaso-motor nerves of the liver. The condition seems to result from a failure on the part of the liver to act as a storehouse for glycogen, a sufficient amount of sugar being thrown into the circulation to secure its excretion by the kidney. We shall return to this subject later on, however, when we consider the glycogenic function of the liver. The *prima facie* indications of glycosuria are characteristic as far as the urine is concerned. The quantity excreted is great, it may be as much as 10 or more litres, *i.e.*, 10,000 c.c., as contrasted with the normal 1500 c.c.; the specific gravity is high—1030 to 1040; and it is of a very pale yellow colour, the paleness being due to the quantity of water rather than to a diminution of the total pigment, while the increased specific gravity is due to the presence of sugar.

The tests for sugar in the urine are founded on its power of reducing cupric sulphate in alkaline solution, its union with phenyl-hydrazin to form phenyl-glucosazone, and its fermentation under the influence of yeast to yield alcohol and CO_2. *Trommer's test* is the most generally useful for qualitative detection. To a little of the urine in a test-tube a few drops of weak sulphate of copper solution are added, followed by excess of sodium hydrate. If the upper part of the blue solution be boiled, a yellow or red precipitate of the lower oxide occurs, which contrasts strikingly with the blue of the unboiled solution beneath it. The same test may be carried out with *Fehling's solution*, which is an alkaline solution of potassio-tartrate of copper, prepared by mixing a solution of copper sulphate with an alkaline solution of Rochelle salt (double tartrate of potash and soda). The Fehling should be freshly prepared, as racemic acid is formed from the tartaric acid, and can itself reduce the cupric oxide. Before using, therefore, it is customary to boil the Fehling, when, if it remains clear, it may be taken to be in good condition. The test is performed in the same way as Trommer's, by adding a little urine to some of the Fehling in a test-tube and heating the upper part of the fluid as before, when the red or yellow precipitate of the lower oxide of copper indicates the presence of sugar.

Phenyl-hydrazin combines with the three reducing sugars—dextrose, maltose and lactose—to form osazones, which differ from each other in their crystalline characters, in their melting point, and in their solubility, and so enable us to distinguish between the sugars from which they are produced. When phenyl-hydrazin is employed for the detection of dextrose in urine, the test may be carried out as follows:—A little phenyl-hydrazin and sodium acetate are added to the urine in a test-tube, and this is placed in a boiling-water bath for half-an-hour. On cooling, bright, canary-coloured, needle-like crystals of phenyl-glucosazone may be identified under the microscope. They melt at a temperature of 205°C.

The *fermentation test* may be employed to confirm the presence of sugar as distinguished from other reducing substances, and is carried out in the following way:—A test-tube is half filled with the suspected urine, a little yeast added, the tube filled up with mercury, inverted in a basin of mercury, and left in a warm place for twenty-four hours. If sugar be present it undergoes fermentation, splitting up into alcohol and carbonic acid, thus:—

$$\underset{\text{Dextrose.}}{C_6H_{12}O_6} = \underset{\text{Alcohol.}}{2C_2H_6O} + \underset{\text{Carbonic Acid.}}{2CO_2}$$

The carbonic acid accumulates in the tube and the urine no longer reduces copper sulphate, or to a very much smaller degree. This test may be employed also quantitatively, 100 parts by weight of CO_2 corresponding to 204·5 parts of sugar.

The *quantitative estimation of sugar* in urine, however, may more conveniently be effected by *titration with Fehling's solution.* Of the latter 10 c.c. are placed in a white porcelain capsule and diluted with five or ten times its quantity of water, so that changes in colour may more readily be seen. Of the urine 5 c.c. are diluted with 95 c.c. of water and the mixture placed in a burette over the porcelain capsule. The diluted Fehling is boiled and the urine is run into it from the burette in instalments, the fluid being reboiled after each addition. This is continued until not a trace of the original blue colour remains, the cuprous oxide being deposited as a reddish powder, and the supernatant liquid changed to a straw-yellow colour. Now, 10 c.c. of Fehling's solution are decolorised by ·05 grm. sugar. If 50 c.c. have been run in from the burette, these 50 c.c. contain ·05 grm. sugar. But the urine was diluted twenty times, so that 2·5 c.c. of undiluted urine will contain ·05 grm. sugar. If the patient has passed 3000 c.c. in the twenty-four hours, and the sample tested was taken from the mixed urine for that time, then $\frac{3000}{2\cdot5} \times \cdot05$ = 60 grms. of sugar.

Fehling's solution may be prepared by dissolving 34·64 grms. of cupric sulphate in 200 c.c. of distilled water, and 173 grms. of Rochelle salt in 600 c.c. of a 14 per cent. solution of caustic soda. The two solutions are then mixed and the mixture diluted to a litre. As already stated, it is apt to decompose, and the stock should therefore be kept away from the light, and always tested by boiling before use.

Another method of estimating the amount of sugar in urine is by the *polarimeter*, the extent of rotation of the plane of polarisation of a ray of polarised light (*e.g.*, yellow) of given wave length passing through the urine being noted. In other words, the amount of rotation is directly proportional to the amount of sugar present in the solution, and is read as an indication of it. But the volumetric method with Fehling's solution, as given above, will be found the most generally useful.

Blood in the urine.—Blood in the urine, or *hæmaturia*, may be the result of effusion of blood from any part of the urinary tract —*e.g.*, kidney, ureter or bladder. The urine, when acid, as it usually is, has a "smoky" appearance if the quantity of blood is small, varying to deep red when the quantity is great. The microscope will reveal the presence of the blood-corpuscles, and

the spectroscope the usual oxyhæmoglobin bands when the blood is fresh. If the urine be exposed for some time it becomes of a dark brown colour, and the hæmoglobin changes to methæmoglobin. On the addition of a drop or two of freshly prepared tincture of guaiacum and ozonic ether to urine containing blood, a blue colouration indicates its presence, but it is to be noted that other substances acting as oxygen-carriers, *e.g.*, fresh vegetable protoplasm, will give the same reaction. *Hæmoglobinuria* differs from hæmaturia in that the hæmoglobin appears in the urine apart from the presence of any blood-corpuscles. It is due to a disintegration of the blood-cells within the blood-vessels, as when the blood of one animal is transfused into the vascular system of another. It also occurs in cases of severe burns, after decomposition of the blood in certain diseases, such as pyæmia and purpura, and, periodically, in what is known as paroxysmal hæmoglobinuria. The urine shows the spectra of oxyhæmoglobin and methæmoglobin.

Bile in the urine.—The urine in jaundice is of a dark brown or greenish colour, due to the presence of bile pigments. These may be recognised by *Gmelin's test.* If impure yellow nitric acid be added to the solution containing the bile pigments, a play of colours is observable at the junction of the fluids, passing from green, through blue, violet and red to yellow. The reaction may conveniently be performed by bringing the urine and reagent together on a white porcelain slab. The blue is due to bilicyanin, the first oxidation product of biliverdin, and the other colours to subsequent stages in the oxidation process (page 13). *Pettenkofer's test* for bile acids is not usually successful with icteric urine when carried out in the ordinary way, but the following method is said to yield satisfactory results:—"Warm a thin film of urine and cane-sugar solution in a flat porcelain dish. Then dip a glass rod in strong sulphuric acid and draw it across the film. Its track is marked by a purplish line" (Halliburton).

The Secretion of Urine.

If we recall the structure of the tubules of the kidney, it will be apparent that the organ differs markedly from other secretory glands in the fact that in addition to the secreting epithelium proper, which we saw lined the convoluted tubules, the broad limb of Henle, and the irregular tubule, it possesses a system of glomeruli which have invaginated the expanded ends of the tubules, and are hence covered by the epithelium of this part of the tubule, which is flattened and does not exhibit the ordinary

secretory character. We should conclude from this that the work of secreting the urine is shared between these two parts of the kidney—the secretory tubules proper and the glomeruli—each of which has its alloted task. And while we should assign from anatomical considerations to the tubules a secretory function analogous to that of an ordinary secreting gland, the structure of the glomeruli and their relation to the flattened epithelium investing them would suggest that here we have to do with a form of secretion having a special relation to the flow of blood through the kidney, and of a simpler nature than that associated with the rodded epithelium of the tubules. It was from such considerations as these that the original "**vital**" theory of Bowman was deduced, namely that the essential constituents of urine, such as urea, were secreted by the tubules, while the water and diffusible salts were separated from the blood by a process of filtration in the Malpighian bodies. In opposition to this, Ludwig supposed that all the constituents of the urine passed through the glomeruli by filtration, and assigned to the tubules the comparatively unimportant function of reabsorbing some of the water, and perhaps of other constituents, to account for the difference in the proportion of salts and urea in the urine and in the blood. He recognised the fact that the efferent vessel of the glomeruli is of smaller calibre than the afferent, and that this would lead to a greater pressure in the glomerular than in ordinary capillaries, and also that the second capillary system beyond the efferent vessel would favour the same result. In fact, he was impressed with the mechanical features of the glomeruli, which seemed eminently suited for filtration processes under varying conditions of blood-pressure; and his view has therefore been termed the "**mechanical**" theory of urinary secretion, as opposed to the vital theory of Bowman, which at least recognised the secretory activity of the tubules. We shall refer to this question later, and it need only be said here that the powers of "selection" exhibited by the kidney are totally inexplicable by any simply mechanical theory, and the balance of evidence is decidedly in favour of the principle of "vital" action; indeed, Bowman's original suggestion is hardly "vital" enough, for even the passage of water and other substances through the glomeruli cannot be regarded as explicable by the laws of filtration and diffusion alone, but is regulated by inherent powers of selection and rejection possessed by the flattened epithelial cells. At the same time, it is true that the activity of the cells is specially related to increase or decrease in the blood-pressure, and consequently of the flow of blood through the kidney, and before proceeding further with the

consideration of renal secretion it will be well for us to see in a little detail how these vascular changes may be brought about.

The *vaso-motor nerves of the kidney.*—Changes in the volume of the kidney, and these imply changes in the calibre of the small renal vessels, as the result of section or stimulation of the renal nerves, are conveniently studied by means of *Roy's oncometer*, which is virtually a plethysmograph adapted to the kidney, the resulting tracing being called an *oncogram*. The apparatus is figured on page 218, and need not be described again here. If a tracing be taken of a kidney in a perfectly normal condition some such result is obtained as is shown in Fig. 283. It will be seen that the kidney curve corresponds very closely with the ordinary blood-pressure curve, showing not only the variations in mean arterial pressure due to respiration, but also the effect of each individual heart-beat.

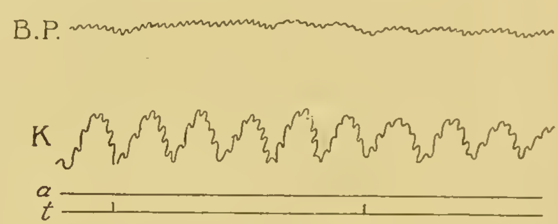

Fig. 283.—TRACING SHOWING BLOOD-PRESSURE AND KIDNEY CURVES.

B.P., Blood-pressure curve; *K*, curve of volume of kidney; *a*, abscissa; *t*, time in quarters of a minute.

In using this instrument for the study of the vaso-motor supply of the kidney, we have to bear in mind a few facts with which we have already become acquainted concerning the local and general effects of arterial constriction and dilatation. The blood-pressure and flow of blood through the capillaries and small vessels of any particular area may be increased not only by a dilatation of the artery supplying the area, but also by a rise in the general blood-pressure, whether it be due to increased cardiac force or constriction of the arteries supplying areas other than the one in question. In the same way, the blood-pressure and flow of blood in any area are diminished not only by constriction of the artery supplying the area, but also by a fall in the general blood-pressure, whether due to a diminution of the cardiac force or a dilatation of the arteries to areas other than the one in question.

It will be at once apparent that different results will ensue if the change in local or general pressure is counteracted by general or local changes. Thus, even if the blood-pressure is raised in the abdominal aorta by constriction of the arteries generally, this will not cause an increase in the size of the kidney if the renal arteries themselves are sufficiently constricted at the

same time. This state of affairs is illustrated in stimulation of the spinal cord after it has been divided below the medulla, which results in a general rise in blood-pressure owing to arterial constriction; but the renal arteries are also constricted, and sufficiently so to reduce the flow of blood through the kidney and cause the organ to shrink. If, however, the nerves of the renal plexus have been previously cut so as to exclude the vessels of the kidney from the general constriction, then, on stimulating the spinal cord as before, the kidney will enlarge owing to the greater amount of blood flowing through it. Again, when the cord is divided below the medulla the renal vessels dilate, and this should lead to an increase in the flow of blood through the capillaries of the area supplied by them, and a consequent increase in the size of the kidney; but the effect of dilatation of the renal vessels is more than counterbalanced by the dilatation of the peripheral vessels of the body generally, and the flow of blood through the kidney diminishes. If other conditions, however, remain the same, dilatation of the renal vessels will lead to increase in the volume of the kidney and the flow of blood through it, and constriction of the renal vessels to shrinking and diminished flow.

The kidney is supplied by both vaso-constrictor and vaso-dilator nerves, but there is as yet no evidence of the existence of secretory fibres such as supply the salivary glands. The variations in the rate of urinary secretion following section or stimulation of the renal nerves can be explained by the resulting changes in the local blood-pressure, and consequently in the rate of blood flow in the vessels of the kidney. The renal nerves form a plexus around the arteries, which they follow to their ultimate subdivisions. As they surround the arteries they give off fine branches, which may be distributed to the convoluted tubules and Malpighian bodies, possibly as secretory nerves. Some of these branches appear to terminate in a "knob" (Berkely).

There seems no reason for supposing (except the desire to do so) that the afferent arterioles of the glomeruli alone are subject to nervous influence and not the efferent vessels. Both are probably under the same control, a supposition which is perfectly in accordance with the theory that the rate of blood flow, and not the intraglomerular pressure, determines the amount of urinary secretion. But to this we shall return later.

The vaso-motor fibres in the dog are found, as the result of experiments with the oncometer, to leave the spinal cord by the anterior roots of the spinal nerves from the sixth dorsal to the second lumbar, but especially by the eleventh, twelfth, and

thirteenth dorsal. Passing through the sympathetic ganglia they run in the splanchnics to the renal plexus and so to their distribution. The vaso-constrictors predominate, so that ordinary stimulation of the nerve roots leads to constriction of the vessels and shrinkage of the kidney, but if the stimulation be infrequent it elicits the action of the vaso-dilators and the kidney swells. The results are more marked either in the way of constriction or dilatation when the roots of the eleventh, twelfth, or thirteenth nerves are stimulated than in the case of the roots higher up, for the effect is more limited to the kidney. When the higher roots are stimulated, the local effect on the kidney tends to become neutralised owing to the effect on other abdominal organs, whereby the general blood-pressure is raised or lowered. Section of the renal nerves leads to dilatation of the renal vessels and increased flow of blood through the enlarged kidney.

Puncture of the floor of the fourth ventricle in the neighbourhood of the vaso-motor centre, by destroying the part of it presiding over the renal vessels, causes their relaxation and a copious flow of urine (polyuria).

Renal secretion.—If a canula be tied in the ureter, it is found that the swelling of the kidney is accompanied by an increased flow of urine and its shrinking by a corresponding decrease in its flow, leading us to the conclusion that secretion by the kidney is in a special way related to the flow of blood through the organ. We have seen that the kidney may probably be divided into two parts as far as its secretory activity is concerned, a *glomerular* and a *tubular* one, and it is the former of these which is especially susceptible to vascular changes and acts as a filtering apparatus—the word filtering being used in a general rather than a scientific sense; for we shall see that secretion by the glomeruli is a much more complex matter. With regard to the tubular secretion of the kidney, there does not seem to be any reason for supposing that it is affected otherwise by flow of blood than the secretion of any ordinary secreting gland. The character of the epithelium and the relation of the blood-stream present no special features to differentiate it to this sense, and, moreover, a secretion of urine may be artificially obtained after the flow of urine has been stopped by section of the medulla. When the cord is divided below the medulla, the pressure falls and the secretion of urine is diminished or comes to an end, but the injection of diuretics, such as urea or sodium acetate, induces a fresh secretion. Nor is the experiment invalidated by the fact that a concomitant dilatation of the small arteries of the kidney and expansion of the organ takes place, for the local dilatation is not proportionate to the

flow of urine. It, indeed, merely accompanies the activity of the secretory cells as it does in the case of the salivary glands—as a favourable condition of secretion without being the cause.

The following experiment by Nussbaum is of great interest in connection with the question of the parts taken by the glomeruli and tubules respectively in the excretion of the constituents of the urine. In frogs the kidney has a double vascular supply. The renal artery gives off arterial branches to the glomeruli, while the renal portal vein, derived from the femoral, breaks up into intertubular capillaries which are in communication with the efferent vessel of the glomeruli. If the renal artery be tied, the blood-supply to the glomeruli is cut off and we are able to study the action of the tubular secreting portion of the kidney alone. If urea be now injected it gives rise to the secretion of urine, and hence we conclude that the tubules secrete urea and water, the secretion of water being a concomitant of the secretion of urea as it is of other secretions. Again, if peptones, sugar or egg-albumin are injected, these are no longer excreted, though they quickly appear in the urine after injection if the renal arteries are not tied. From this we conclude that these substances are passed into thc urine through the glomeruli.

There may be an anastomosis between the two sets of vessels, as asserted by Adami, but its importance is certainly not sufficient to invalidate the experimcnt.

The secretory activity of the tubules, and by this we mean the parts of them with "rodded" epithelium, is further demonstrated by the important experiments of Heidenhain. If the spinal cord be divided below the medulla in order to reduce the blood-pressure and arrest the flow of urinc and sodium sulphindigotate injected, the animal killed after a variable time, and the kidney examined, it will be found that the pigment has passed into the cells of the rodded epithelium and the lumen of the tubules of which it forms the wall. As there was no flow of water owing to the section of the medulla, the pigment remains much where it was when thrown out of the cells into the lumen of the tubes, and none is found in the glomeruli or Malpighian capsules. From this we conclude that the tubules in question do excrete certain substances. If now the same experiment be performed, except that the cord is not previously cut, we find on subsequently examining the kidney that the blue is found in the medulla generally as well as the cortex, though in the non-rodded portions of the tubules it is found in the lumen only, and not in the cells. From this we conclude that when the blood-pressure is normal, the

water poured out from some part of the tubule—whether it be the terminal part enveloping the glomerulus or the rodded cells of the convoluted tube, &c.—has washed the pigment towards the medulla. The third part of the experiment consists in the cauterisation of a part of the cortex of the kidney with nitrate of silver previous to injection, the cord being uncut. Here only the cortex is blue where the nitrate has been applied, the pigment being in the rodded cells as before. Elsewhere, both the cortex and medulla are blue. From this we may conclude that most of the water is passed by the glomeruli, for cauterisation has not destroyed the power of the rodded epithelium to excrete the pigment granules, and probably would not have destroyed its power to excrete water if it had possessed it to any great extent.

In this connection it may also be mentioned that in birds and serpents with semi-solid urine, the glomeruli are smaller than in mammals. Crystals of uric acid have been observed in the epithelium of the convoluted tubules of birds.

By the above experiments, then, we confirm our *prima facie* impression that there is a *glomerular* and a *tubular* secretion, and, furthermore, conclude that normally the glomeruli give passage to most of the water and salts of the urine, while the rodded epithelium of the tubules is concerned with the more complex function of the excretion of urea and other nitrogenous metabolites.

Secretion by the kidney differs from the ordinary secretion of glands in that the substances secreted are merely withdrawn, or picked out as it were, from the blood, and are not the result of elaboration by the secreting cells themselves.* For this the reason is to be found in the fact that the urinary constituents are in the nature of waste products, and are not intended for future use by the economy. We may appropriately enough, therefore, speak of the urine as an "excretion" rather than a "secretion" in the ordinary sense of the word.

We may now turn to the consideration of glomerular and tubular secretion in a little detail.

Glomerular secretion.— We have seen that the vascular expansion of the kidney is accompanied by an increased flow of urine; and in an earlier chapter it was stated that dilatation of a small artery, other conditions remaining the same, results in an increased and more rapid flow in the capillaries supplied by it, and a rise in the pressure within them. What effect then does this state of affairs in the glomerular tuft have

* Except in the case of hippuric acid (which is formed from benzoic acid and glycin, the combination taking place in the kidney) and some other substances.

on the secretion of urine? Is the increased secretion the result of the more rapid flow of blood through the capillaries, or the increase of pressure within them, or both these factors?

That increased pressure alone will not account for it is shown by the fact that if the venous outflow by the renal vein be partially obstructed, the secretion of urine, instead of being increased, is diminished, and if the obstruction be complete is arrested altogether, although the pressure is enormously increased, so that we cannot regard the passage of fluid through the walls of the glomerular tuft in the same light as that through an ordinary capillary wall to form lymph. In the latter case, as we have seen, the transudation is directly affected by pressure. And, furthermore, in this connection it may be pointed out that whereas in the case of the ordinary capillary the constituents of the blood generally pass through its wall, in the case of the glomerular tuft only water and certain diffusible substances escape from it, and under ordinary conditions none of the serum-albumin and globulin. The process is clearly not one of simple filtration under pressure, and the selective power shown we may attribute to the fact that we are not dealing with the capillary wall alone, but *plus* the covering of flattened epithelial cells of the expanded end of the uriniferous tubule.

The rapid flow of blood through the capillaries of the tuft, which is a condition of secretion, would favour diffusion; and we know that many of the constituents of the urine, *e.g.*, salines, are readily diffusible, and also by the experiment on the amphibian kidney that diffusible substances, such as sugar and peptone, pass into the urine through the glomeruli. We might therefore, at first sight, be inclined to assign to diffusion a master rôle. But this is at once discountenanced by the fact that while egg- and serum-albumin differ but slightly in their diffusibility, when they are injected into the blood-stream they meet with a different fate, the former being at once excreted in the urine as a foreign body, while the latter is retained. Moreover, if diffusibility was the paramount consideration, how could we account for the fact that urea—a most diffusible substance—passed through the tubules of the kidney and not through the glomeruli?

The epithelium of the glomerular tuft may be injured by temporarily ligaturing the renal artery, and so depriving it of its blood-supply. The secretion of urine is then stopped, and when the ligature is removed the urine which is first secreted is found to contain serum-albumin and globulin. In other words, the epithelium, which normally afforded an efficient barrier to the passage of these substances from the blood into the urine, in its

injured condition can no longer do so; and the same state of affairs may result from kidney disease. But even under such circumstances it does not entirely lose control, for the albumin and globulin do not pass through it in the proportion in which they are present in the blood or in accordance with their diffusibility.

These considerations, therefore, bring us to the conclusion that the passage of substances through the glomerular epithelium is not governed either by filtration or diffusion, though these two factors may play their part. The "vital activity" of the cells covering the glomerular tuft is the dominant element, the physical processes being controlled and directed by it.

Secretion by the tubules.—We have said that the kidney for the most part merely picks out as it were from the blood-stream the waste substances already present there, and in this way contrasts with such glands as the salivary and gastric and the pancreas, the specific constituents of whose secretion are elaborated in the gland-cells themselves. This may readily be shown by the simple experiment of extirpating the glands and noting whether the specific constituents of their secretion accumulate in the blood. Removal of any of the three glands named leads to no accumulation in the blood of either ptyalin, pepsin or trypsin. These substances, the result of the activity of the gland-cells themselves, and not pre-existing as such in the blood, are simply no longer formed when the gland which produces them is removed from the economy. Just in the same way, if the liver be removed, there is no accumulation in the blood of either bile acids or pigments. With the kidney, however, it is different. If these organs are removed, urea, the chief substance eliminated by them, accumulates in the blood. In other words, the urea is not formed in the kidney itself but results from metabolic changes elsewhere, and is merely excreted or withdrawn from the blood as it flows past the secreting epithelium of the tubules.

In birds and reptiles whose nitrogenous excretion is mainly in the form of uric acid, a corresponding accumulation of this substance in the blood results when the kidneys are removed.

In the case of hippuric acid, which has already been referred to, the cells seem, however, to play a part in its formation. We have seen that it results from the combination of benzoic acid with glycin (page 423), and if benzoic acid be given by the mouth or injected into the blood-stream, hippuric acid appears in increased quantity in the urine; and the question arises—Where does the benzoic acid meet with the glycin? In the first place hippuric acid is not present in the blood even in herbivora, the urine of which contains large quantities of it, and our attention is thus

early directed to the kidneys themselves as the possible seat of production; and the following experiments confirm this view:—If an excised "living" or "surviving" kidney be perfused with blood containing benzoic acid and glycin, hippuric acid is found in the blood issuing from it. And it is not essential even that the glycin should be provided, benzoic acid alone leading to the production of hippuric acid. Furthermore, if a live kidney be merely cut in pieces and benzoic acid mixed with them, hippuric acid is formed, so that we conclude that the cells of the tubules combine the benzoic acid brought to them by the blood-stream with the glycin they contain as the result of their own metabolism, and that in this manner the hippuric acid of the urine is produced.

Mere admixture of the benzoic acid and glycin with blood will not effect the synthesis, nor will this take place in the above experiments unless the kidney has been but recently removed from the body and still retains its vitality.

Other substances also may reappear in the urine combined with glycin, and in these cases, also, the combination probably takes place in the cells of the secreting tubules. Probably, also, the cells of the tubules may be to some extent responsible for the final form in which the urinary pigments derived from the hæmoglobin of the blood directly, or indirectly through the biliary pigment, appear in the urine. In frogs, acid sodium phosphate appears to be produced by the cells of the tubules.

Diuretics increase the urinary secretion. Many of them, such as urea, caffein, sodium acetate and potassium nitrate, appear to produce their effect by directly stimulating the renal epithelium, the accompanying dilatation of the vessels being, as in the case of salivary secretion, not the cause of the glandular activity but a favourable circumstance attending it. Digitalis, on the other hand, is a diuretic whose action appears mainly to depend on its effect on the blood-pressure. It increases the force of the heart beat and at the same time constricts the peripheral arterioles, both factors increasing the pressure. The constriction of the renal vessels themselves, however, may be sufficient to counteract the general rise in pressure, and digitalis acts more constantly in disease than in health. Its action in disease may be explained, perhaps, as due to the increase of cardiac force raising the blood-pressure independently of any constricting influence on the arterioles.

Among other conditions affecting the quantity of the urinary secretion we may refer shortly to the effect of the state of the cutaneous vessels and of the nervous system. If the body is exposed to cold the secretion of sweat is stopped, the vessels of the skin being constricted. This constriction is balanced by an

accompanying dilatation of the vessels of the kidneys and other abdominal viscera leading to an increased flow of blood through the kidneys and an increased secretion of urine. On the other hand, if the cutaneous vessels are dilated, as when the body is exposed to warmth, the secretion of sweat is promoted, while the vessels of the kidneys and abdominal viscera generally are proportionately constricted and the flow of urine is diminished.

In the matter of the discharge of water, therefore, the skin and kidney may be regarded as complementary to each other.

The effect of the condition of the central nervous system upon urinary secretion is shown by the increased secretion which takes place under the influence of excitement, fear, &c. In hysteria, the quantity passed may be enormous and consist of little more than water, suggesting that here the activity of the glomeruli is especially brought into play.

Estimation of renal work.—Perhaps the most powerful argument against the purely mechanical theory of urinary formation is to be found in a study of the relative osmotic equivalents of urine and blood plasma, and a computation of the amount of actual work necessitated in the separation of the 1500 c.c. of urine passed in the day. In one instance mentioned by Dreser the plasma had an osmotic pressure equal to ·92 per cent. NaCl solution; whilst that of the urine was equal to 4 per cent. saline. In this case 37 kilogrammes of work must have taken place to separate the urine from the plasma.

To recapitulate the conclusions we have arrived at in the preceding section, we may say that most of the water and salts of the urine pass through the glomeruli, the process being a true secretion and not a mere filtration. Sugar, peptone and egg-albumin when injected into the blood-stream are passed through the same channel. Some of the water and salts with the urea and other characteristic organic constituents of the urine are excreted by the rodded epithelium of the tubules. The secretion of urine varies with the blood-pressure in the renal vessels—a high pressure accompanied with a full and rapid stream of blood through the vessels of the kidney leading to an increase in the secretion, and a low pressure, &c., to a decrease. It is probably not the pressure itself, but the velocity of flow which is the determining factor. The kidney is supplied with vaso-constrictor and vaso-dilator nerves, but no secreting fibres have yet been demonstrated. Diuretics act either directly on the secretory epithelium or by increasing the blood flow. The skin and kidney are complementary to each other in the discharge of water.

The Discharge of Urine—Micturition.

Structure of the ureter.—The ureter or duct of the kidney is about the size of a goose quill in diameter, from twelve to sixteen inches in length, and extends from the pelvis of the kidney (which forms its upper expanded extremity) to its opening into the bladder, which it enters obliquely. It is lined by a layer of transitional epithelium, continuous with that lining the pelvis of the kidney and calyces and reflected over the papillæ, where it joins the epithelium of the discharging tubules. The epithelial layer rests upon fine connective tissue, the two together constituting the mucosa, which is thrown into longitudinal folds in the undistended condition of the tube. Further out, the connective tissue becomes looser, and forms a submucosa separating the mucosa from the muscular coat. The latter consists of three layers of non-striped fibres—internal, middle and external. The fibres of the middle coat run circularly, those of the internal and external coats longitudinally. Only the middle coat is present in the pelvic expansion, and the external coat is only found in the lower part of the ureter towards the bladder. The middle coat is the thickest of the three. Outside the muscular coat is an adventitia of connective tissue.

Nerve-fibres pass into the upper end of the ureter from the renal plexus, and into the lower end from the spermatic and hypogastric plexuses. The nerve-fibres are both medullated and non-medullated, and nerve-cells are found amongst them; but there are said to be neither nerve-cells nor nerve-fibres in the middle part of the tube between the ends.

The obliquity of the opening of the ureter into the bladder serves as a valve to prevent the reflux of urine when the viscus is distended.

Structure of the bladder.—The bladder is lined by transitional epithelium continuous with that of the ureters, and here also, in the contracted state of the viscus, the epithelium, with the fine connective tissue beneath it constituting the mucosa, is thrown into folds which disappear on distension. Beyond the mucosa proper the connective tissue becomes looser, and may be regarded as a submucous layer. Outside this is the muscular wall proper of the bladder, consisting of flattened or rounded bundles of non-striped fibres arranged in a plexiform manner. These bundles in their disposition may be divided into three layers: an inner, running longitudinally, which is continuous with the same layer in the ureters and is very thin; a middle circular one, corresponding

with the same layer of the ureters, and thicker; and an external longitudinal layer, the longitudinal arrangement being more obvious at the front and back of the bladder than on the sides. This outer longitudinal layer is continuous with the corresponding layer in the ureters, and is sometimes known as the *detrusor urinæ*. The middle coat is especially thickened round the opening of the urethra, and the term *sphincter vesicæ* is sometimes applied to this part of it. But neither of these terms appear to be justifiable. The three layers described probably represent physiologically a single or common hollow muscle whose function it is to diminish the size of the bladder uniformly and secure expulsion of its contents. The muscular wall of the bladder is bounded on the outside by a layer of connective tissue, which is in its turn covered, over a considerable portion of the organ, with peritoneum. The nerves to the bladder are supplied by the hypogastric plexus, and appear to be derived (1) from the lower dorsal and upper lumbar cord through the sympathetic and (2) directly from the sacral nerves. There are both medullated and non-medullated fibres, numerous nerve-cells being found among them, and both cells and fibres are more numerous about the neck of the bladder.

The **urethra** is lined by a layer of epithelium, which is transitional where it traverses the prostate, columnar in the body of the penis, and stratified squamous at the meatus. The proper *sphincter urethræ*, which, as we have seen, is not the so-called sphincter vesicæ, which is merely an integral part of the muscular wall of the bladder, consists of a layer of muscular fibres, both striped and non-striped, surrounding the prostatic portion of the urethra, which represents the sphincter vesicæ externus of Henle, and is under the control of the will.

Micturition.—The urine is secreted continuously, though at a varying rate. It is collected from the discharging tubules of the kidney into the pelvis, and thence passes into the ureter, down which it is propelled partly by the action of gravity and partly by intermittent peristaltic contractions of the tube. It then collects in the bladder, its return to the ureters being prevented by the valve-like character of their orifices, until it is discharged usually as the result of a voluntary effort. Previous to this effort the urine is retained in the bladder owing to the tonic contraction of the sphincter vesicæ externus, to which reference has already been made. As the urine collects in the bladder we become conscious of its distension, leading us to make an effort in which the wall is thrown into ill-defined peristaltic contraction, and the sphincter overcome, or more probably even relaxed. As

the urine passes along the urethra, its passage is accelerated by the rhythmical contractions of the ejaculator urinæ. Contraction of the abdominal muscles accompanies the act of micturition as it does that of defæcation, and by pressure on the bladder assists in the discharge of its contents.

It may be added, *en passant*, that the desire to make water appears not to be dependent so much on the quantity of fluid in the bladder as on the pressure exerted by the fluid on the bladder wall. Thus when the bladder is in a state of "tonic" contraction a smaller amount of fluid within it will occasion as much pressure on the mucosa as a larger quantity when the tone is not so marked.

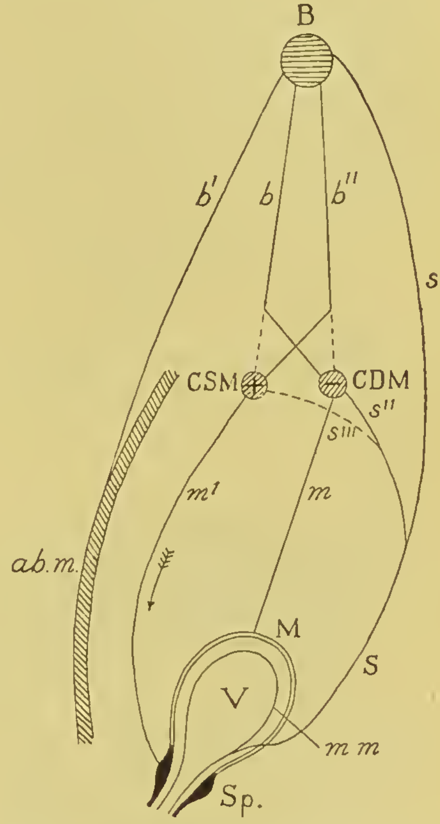

Fig. 284.—Scheme of Parts Concerned in Micturition while at rest.

V, Bladder; *Sp*, sphincter; *M*, muscular wall; *mm*, mucosa; *m*, nerve to muscular wall (detrusor urinæ) from *CDM*, detrusor centre in spinal cord; *m'*, nerve from the centre *CSM* in spinal cord to sphincter muscle *Sp*; *B*, brain; *b* and *b''*, nerve filaments from brain to spinal centres; *b'*, nerve to abdominal muscles; *S*, *s'*, *s''*, *s'''*, nerve from mucosa of bladder to spinal centres and brain.

The nervous mechanism involved in the act of micturition appears to consist of a spinal reflex centre which may be set in action by impulses from the brain alone, from the bladder alone, or, as is usually the case, from both. That such a reflex centre exists in the cord may be inferred from the fact that in a dog in which the cord has been divided at the level of the upper lumbar region, so that no volitional impulses from above can pass, quite normal micturition is carried out as the bladder becomes full, and may even be excited by such slight stimulation as sponging the skin around the anus. Here the act is obviously reflex. The centre is situated at the level of the fifth lumbar nerve, and on appropriate stimulation (1) throws into contraction the wall of the bladder and ejaculator urinæ and (2) inhibits

the tone of the sphincter vesicæ externus. The accompanying Figs. suggest the connections of the centre and the way it is

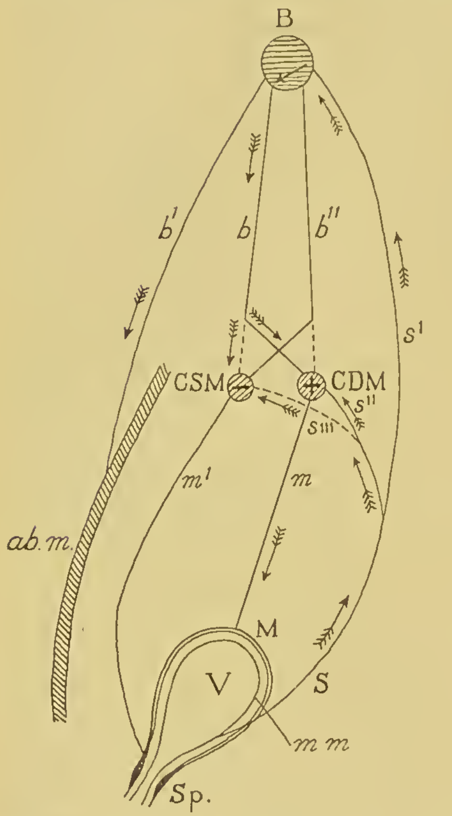

Fig. 285.—Scheme of Parts Concerned in Micturition while in Action.

V, Bladder; *M*, muscular wall; *mm*, mucosa; *m*, nerve to muscular wall, to which impulse now passes from *CDM*, detrusor centre in spinal cord; *m'*, nerve from sphincter centre *CSM* in cord to neck of bladder, along which no tonic influence now passes; *Sp*, sphincter muscle: *B*, brain; *b* and *b''*, nerves to spinal centres, of which the former conveys an impulse strengthening the detrusor centre and inhibiting the action of the sphincter centre; *b'*, nerve to abdominal muscles *ab.m*, carrying impulse to same; *S*, *s'*, *s''*, *s'''*, nerve from mucosa of bladder to spinal centres and brain, now carrying impulse.

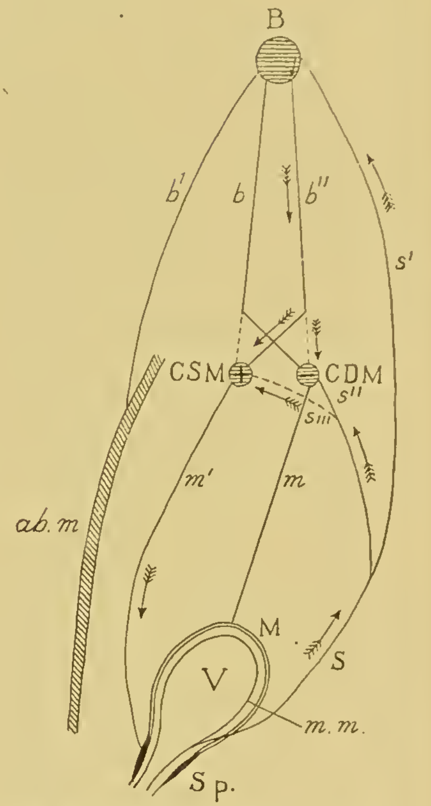

Fig. 286—Scheme of Micturition, showing how the act can be inhibited by a voluntary effort.

Letters as on Fig. 285. Impulse from *B*, brain, passes along *b''*, which inhibits detrusor centre *CDM*, and stimulates sphincter centre *CSM*.

subject to different impulses from the bladder and the brain.

The double nervous supply to the bladder is comparable to that of the rectum, and, like it, appears to have a double action.

Stimulation of the branches of the sacral nerves produces marked vesicular contraction in the dog, in which the longitudinal coat is well developed; while stimulation of the nerves

derived from the dorsal and upper lumbar cord results in less marked contraction, and mainly affects the circular fibres, which we saw were especially developed round the neck of the bladder, and probably serve to complete the emptying of the viscus.

Incontinence of urine occurs when the spinal cord is diseased so that the centre is thrown out of action. In this case the urine accumulates in the distended bladder, and when the resistance to its escape is overcome dribbles away from the urethra *pari passu* with its entrance from the ureters. The so-called incontinence of urine in children has another origin. Here the centre is intact and a true act of micturition is performed reflexly while the child is asleep, frequently as the result of local irritation of the external genital organs and the abeyance of cerebral control.

II.—Excretion by the Skin.

The **structure of the skin.**—The skin is divisible into two main layers—an epiblastic one, the **epidermis**, and one of mesoblastic origin, the **dermis** or **cutis vera**. The epidermis consists of stratified squamous epithelium, and is itself divisible into several layers, of which the stratum Malpighii below, and the stratum corneum above, are the main ones; between them lies the stratum granulosum and stratum lucidum. The dermis is composed of ordinary connective tissue, the superficial part of which, immediately beneath the epidermis, is fine and closely set; while the deeper part is much looser and corresponds morphologically with the submucosa of the stomach and intestines. Free movement between the deeper part of the dermis and the subjacent connective tissue

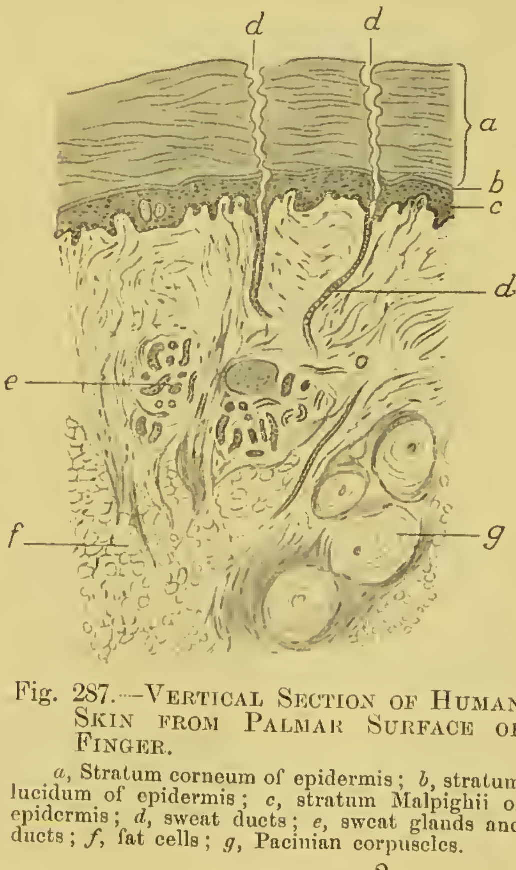

Fig. 287.—Vertical Section of Human Skin from Palmar Surface of Finger.

a, Stratum corneum of epidermis; *b*, stratum lucidum of epidermis; *c*, stratum Malpighii of epidermis; *d*, sweat ducts; *e*, sweat glands and ducts; *f*, fat cells; *g*, Pacinian corpuscles.

can take place, just as the mucosa of the stomach is movable upon the muscular coat.

The *stratum Malpighii* is the deepest layer of the epidermis, and rests upon the surface of the dermis, which is condensed to form a basement membrane. The surface of the dermis is not flat but is raised up into a series of conical papillæ, some simple and some compound, between which the epithelium correspondingly dips down. As in the Malpighian or soft layer of the hard palate, the cells of the stratum Malpighii of the skin are arranged in several layers, and their shape differs at different levels.

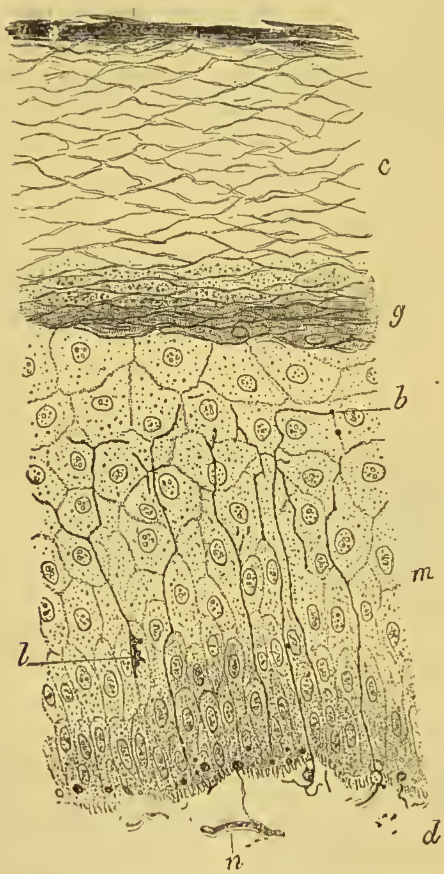

Fig. 288.—Vertical Section of Human Epidermis with terminations of Nerve-Fibrils.

n, Nerve-fibre; *b*, terminations of nerve-fibrils; *c*, stratum corneum; *g*, stratum granulosum; *m*, stratum Malpighii; *d*, dermis.

The deepest cells, *i.e.*, those resting on the basement membrane, are granular, somewhat columnar in shape, and placed vertically to the surface on which they lie. These are the *germinal cells* of the stratum Malpighii, from which those above are to be developed, and they possess a relatively large oval nucleus, which frequently exhibits signs of division. The cells above these forming the greater part of the Malpighian layer are larger, polygonal in shape, with a centrally placed spherical nucleus, and are not so granular. They do not meet each other with plane surfaces, but by short prickle-like processes, and are therefore sometimes termed "prickle cells" (page 38). There is, however, no distinct line of demarcation between them and the germinal cells, and above the prickle cells become flattened rather than polygonal immediately beneath the *stratum granulosum*. The

cells of the latter layer are usually two or three deep, somewhat lozenge-shaped and destitute of prickles. They contain granules of eleidin, which ultimately become the keratin of the stratum corneum. The cells of the stratum granulosum stain deeply with many reagents. Above or external to the last layer is the *stratum lucidum*, a narrow, homogeneous, translucent, refractile band composed of flattened cells fused together. Here and there flattened nuclei may sometimes be made out in it.

It may be noted that neither of these two layers nor the surface of the stratum Malpighii follow the line of the downward prolongations of the stratum Malpighii between the papillæ of the dermis, but lie in a plane corresponding with that of the surface of the skin.

The *stratum corneum*, very thick in some parts, such as the palmar aspect of the fingers, consists of flattened scales or plates composed of keratin, the nuclei of the original cells being only visible now and again. The plate-like cells of this layer are being constantly thrown off at the surface by the process of attrition, and replaced by others from below.

The **dermis** or **cutis vera** is composed of ordinary connective tissue, *i.e.*, of white fibres, yellow elastic fibres and connective tissue cells, which is finely set beneath the stratum Malpighii, but more areolar in character in the deeper part. The larger blood-vessels are found in the deeper, coarser part of the cutis vera, while a fine capillary network extends beneath the epithelium. In the dermis are also found lymphatics, nerves, and their terminations. Of the latter, Wagner's corpuscles oceur in the papillæ and the Pacinian corpuscles more deeply or in the subcutaneous connective tissue. Nerve-fibrillæ pass from the dermis into the stratum Malpighii and terminate there (see page 450). In parts where there is subcutaneous fat, groups of fat cells in varying quantity are found in the deeper part of the dermis and subcutaneous tissue.

In addition to the structures already mentioned, however, two others are also found in the skin, viz., the sweat glands and the hair-follicles. The former, as their name implies, secrete the sweat, while from the latter is derived the sebum of the sebaceous glands.

The **sweat glands** vary in size and number in different parts of the body, but are most numerous in the skin of the palms of the hands and soles of the feet. Here, too, there are no hair-follicles, so that the sweat from these parts contains no admixture of sebaceous matter. They are simple tubular glands, of which the secreting part and the lower end of the duct are much coiled on

themselves, and lie in the deeper part of the dermis, the rest of the duct joining the stratum Malpighii (of which the whole gland is a downgrowth) at the apex of one of the downward prolongations between the papillæ.

The *duct* of the gland, which is somewhat narrower than the secreting portion, has a small regular lumen, and is lined by a double layer of cubical or rounded cells resting on a basement membrane continuous with the surface condensation of the cutis vera. The lumen is continued upwards through the downgrowth of the stratum Malpighii, with which the duct becomes continuous and forms a somewhat corkscrew-shaped passage through the epidermis to open on the surface, the passage becoming wider as the surface is approached.

Fig. 289.—Section of Skin (Human) showing Sections of Sweat Glands and Ducts.

a, Sweat gland (secretory portion) cut longitudinally; *b*, sweat gland (secretory portion) cut transversely; *c*, secreting cells; *d*, non-striped muscle-fibres; *e*, basement membrane; *f*, irregular lumen of secreting portion; *g*, duct; *h*, fat cells; *i*, connective tissue of cutis vera.

The *secreting portion* of the tubule is broader than the duct, and is lined by a single layer of larger and more irregular cells, so that the lumen is irregular, as shown in the figure. The cells, it may be noted, are rather differently affected by staining reagents than are those of the duct. Between the cells and the basement membrane is a layer of non-striped muscular fibres, running longitudinally or spirally. The fibres are, however, discontinuous with each other laterally, as may be seen in a transverse section of a tubule. They are probably concerned with the expulsion of the secretion.

Hair-follicles.—" A *hair* is the development, in the form of a cylinder, of a cap of corneous epithelium surmounting a papilla of the dermis, sunk to the bottom of a tubular pit or involution of the skin, called a hair-follicle" (Foster). Except in certain parts, such as the palms of the hands and the soles of the feet, the body is covered with fine hair, termed the *lanugo*, but the structure of the hair-follicle, as described below, can only be made out in the large

hairs, *e.g.*, of the scalp. Such a hair-follicle consists of the following parts :—

1. A fibrous covering and basement membrane derived from the dermis.

2. Epithelium
- *a.* Outer root sheath.
- *b.* Inner root sheath. { Henle's layer. / Huxley's layer.
- *c.* Hair.

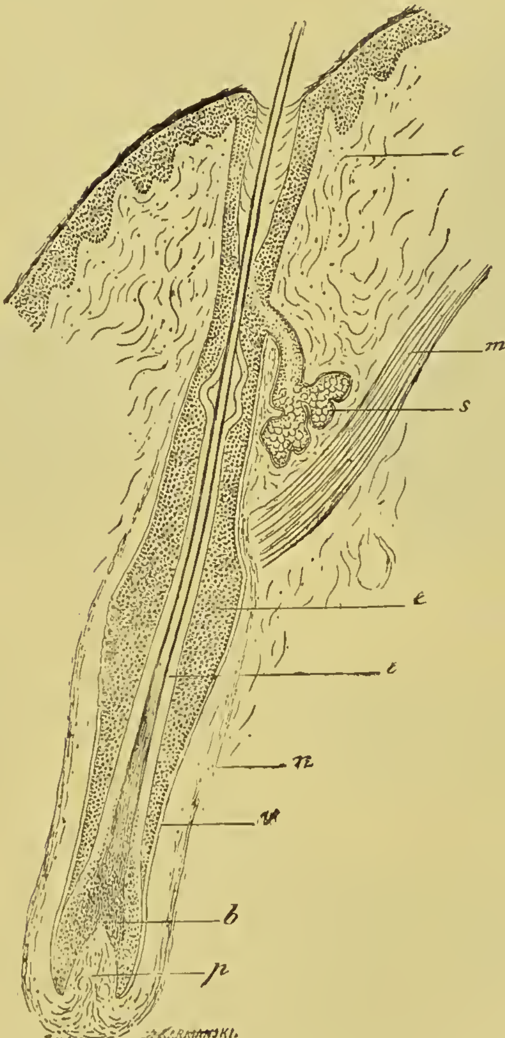

Fig. 290.—Vertical Section of Hair-follicle of Human Scalp.

c, Dermis; *m*, erector pili muscle; *s*, sebaceous glands; *e*, outer root sheath; *i*, inner root sheath; *n*, fibrous covering; *v*, hyaline membrane; *b*, bulb of hair; *p*, papilla.

The *fibrous investment* (Fig. 291, *a*, *b*), continuous with the connective tissue beneath the stratum Malpighii above and the

papilla of the hair-follicle below, consists of two layers—an outer longitudinal and an inner circular supporting a capillary network. The basement membrane between the fibrous investment and the epithelial elements of the hair-follicle is continuous with the surface condensations of the cutis vera beneath the stratum Malpighii of the general skin surface, and is especially developed, being very bright and refractile, with a double contour. It completely invests the epithelial part of the follicle and is known as the *hyaline membrane.*

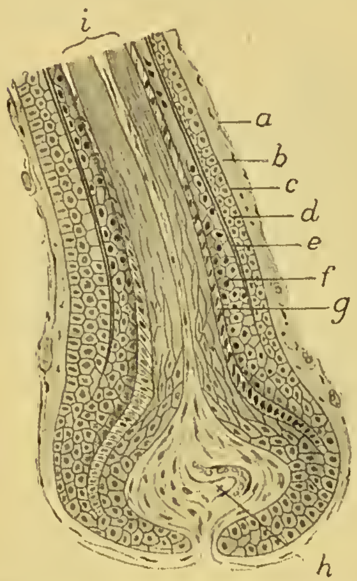

Fig. 291.—Longitudinal Section of Hair-Follicle of Lip of Kitten.

a, b, Inner dermic covering; *c,* hyaline membrane; *d,* outer root sheath; *e,* Henle's layer (inner root sheath); *f,* Huxley's layer (inner root sheath); *g,* cuticle of hair; *h,* papilla of cutis vera; *i,* hair.

The *outer root sheath* (*d*) is continuous with the stratum Malpighii, and is sometimes called the Malpighian layer. It resembles the stratum Malpighii in structure, except that the cells forming it have no prickles. In its broadest part, midway down the follicle (Fig. 293, *c*), the cells are three or four deep, but lower down it narrows considerably. The external cells of this layer will obviously be continuous with the lower or germinal cells of the stratum Malpighii of the skin.

The *inner root sheath* (Fig. 291, *e, f*) is narrower than the outer and is divisible in its lower part into two perfectly distinct layers (Henle's and Huxley's) which are, however, fused higher up. The external layer (Henle's, *e*) is narrow, refractile and homogeneous. It is composed of flattened squames, the rod-shaped (in section) nuclei of which may be made out here and there, but the outlines of the individual cells are rarely discernible. The internal layer (Huxley's, *f*) is composed of small polygonal cells, two or three deep, which stain readily with such a reagent as hæmatoxylin and exhibit deeply-stained, somewhat quadrangular nuclei. Within Huxley's layer is the hair itself. Fig. 292 shows transverse sections of the hair-follicle at different levels. In A the section has been taken at a point where the two layers of the inner root sheath are

fused together; in B at a lower level, where its division into Henle's and Huxley's layer is quite distinct.

The *hair* itself, it is scarcely necessary to say, is cylindrical in shape, and in structure possesses a cuticle, a cortex and a medulla. The *cuticle* consists of flattened non-nucleated scales which are imbricated, that is to say, overlap each other, from below upwards. The main mass of the hair—the *cortex*—is made up of fibrous non-nucleated cells, which have been transformed to keratin, arranged longitudinally and cemented together. The fibrous character of the cells gives an appearance of longitudinal striation to the cortex, and pigment granules are sometimes found between the cells. The *medulla*, when present, is represented by a longitudinal row of quadrangular cells, hollowed out in their interior, and thus appearing black from the air they contain.

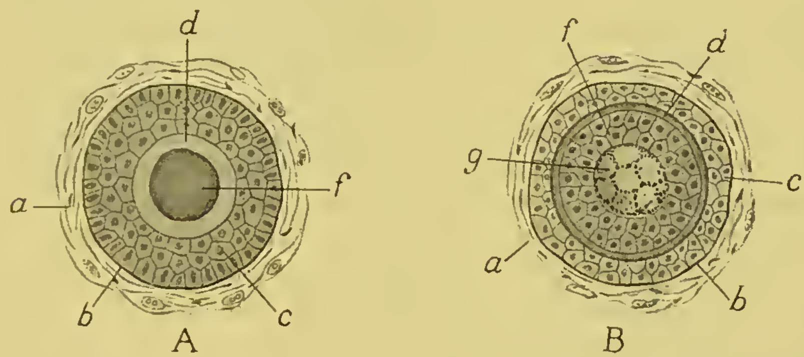

Fig. 292.—Transverse Sections of Hair-Follicles at different Levels.

A, Below opening of sebaceous glands. *a*, Fibrous part of dermic covering; *b*, hyaline membrane; *c*, outer root sheath; *d*, inner root sheath; *f*, hair.
B, Above apex of papilla. *a*, Fibrous dermic covering; *b*, hyaline membrane; *c*, outer root sheath; *d*, Henle's layer; *f*, Huxley's layer and cuticle; *g*, commencement of hair, showing pigmentation.

In addition to the above characters of the hair-follicle and its parts, there are, however, some special features in connection with its structure at different levels which require notice. In the first place, the *sebaceous glands* open into its neck a little below the level of the epithelium of the general skin surface. These are outgrowths from the outer root sheath of the follicle; they are saccular in shape and possess a short duct, into which the alveoli directly open. The basement membrane surrounding the alveoli is continuous with the hyaline membrane and the surface condensation of the dermis beneath the stratum Malpighii of the skin. The cells of the alveoli immediately upon the basement membrane are continuous with the outer cells of the outer root

sheath, and, like them, are low, columnar, or cubical in shape. Within these the cells are more polygonal, while in the centre itself are cells which have fattily degenerated in the process of formation of the sebum, which is the secretion of the gland. The sebum is poured into the neck of the follicle and thence finds its way on to the skin surface, its supply being maintained by proliferation of the peripheral cells of the alveoli as the central ones become used up.

Below the neck, the hair-follicle increases in thickness as it passes downwards, owing to an increase in the thickness of the outer root sheath, but narrows again to some extent before the bulb, the lowest and broadest part of the follicle, is reached.

As the Malpighian layer of the hair-follicle or outer root sheath reaches the bulb (Fig. 291), it becomes narrowed to possibly one layer only of cells, which, when traced downwards, are seen to be continuous with a single layer of cubical or columnar cells immediately above the papilla of the cutis vera—cells which are the continuation of the germinal layer of the stratum Malpighii and lie immediately upon the basement membrane. As the hair reaches the bulb it expands considerably and becomes continuous with the greater part of the two limbs (in section) of the bulb which surround the papilla. The *bulb* is composed for the most part of polygonal cells, amongst which the layers of the hair and its sheaths become lost, as is well seen in the figure. Just above or about the level of the junction of the hair with the bulb, the inner root sheath is at its thickest, and the cuticle of the hair itself is distinctly seen in the form of columnar (in section) cells placed with a slant upon the shoulder of the root of the hair, so that they are imbricated from below upwards.

The hair itself is developed from the germinal cells covering the dermic papilla, between which and its fibre cells there is a gradual transition. When there is a medulla present, it is due to a growth in the centre of the hair of a longitudinal row of cells continuous with the germinal cells, which persist as a central core. In the tactile hairs of some animals, the connective tissue of the papilla itself appears to be prolonged into the hair as a core.

The *papilla* is composed of fine connective tissue supporting a capillary network. Nerve-fibrillæ penetrate the Malpighian layer of the hair-follicle from the dermic covering and the papilla.

The hair-follicles are not placed vertically to the surface of the body but obliquely, as shown in Fig. 293, and the *erector pili* muscle is found in the obtuse angle between the epidermis and the hair-follicle. This is a band of non-striped muscle-fibres which is attached, on the one hand, to the basement

membrane beneath the epithelium of the skin surface, and, on the other, to the hyaline membrane of the hair-follicle above the bulb. When the muscle contracts, the hair naturally stands on end,

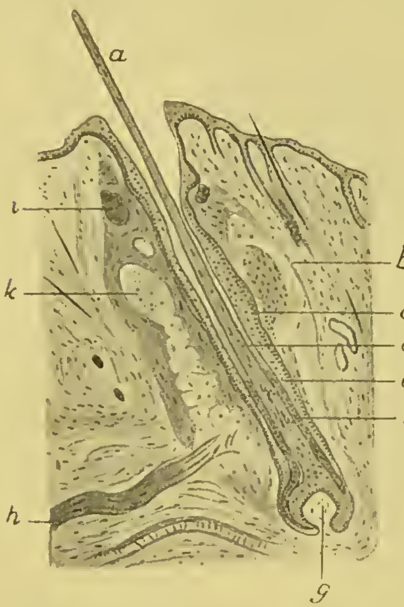

Fig. 293.—VERTICAL SECTION OF LIP OF KITTEN SHOWING TACTILE HAIR.

a, Hair; *b*, outer dermic covering, enclosing sinus (*k*); *c*, outer root sheath (continuous with stratum Malpighii of epidermis); *d*, inner root sheath; *e*, Henle's layer; *f*, Huxley's layer; *g*, dermic papilla; *h*, nerve piercing dermic covering; *i*, sebaceous glands (rudimentary); *k*, sinus between layers of dermic covering.

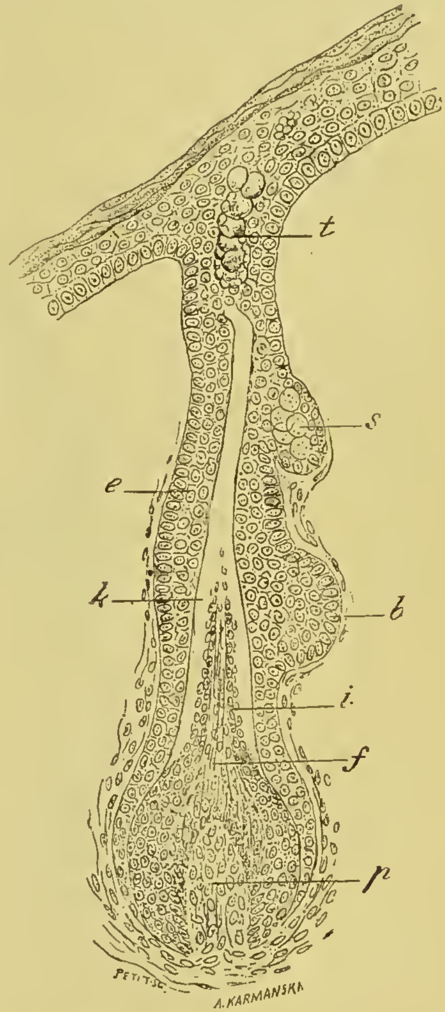

Fig. 294.—DEVELOPING HAIR-FOLLICLE.

p, Papilla; *f*, cells above it proliferating and extending upwards to form the future hair; *i*, cuticle of hair; *k*, inner root sheath; *e*, outer root sheath; *b*, germinal layer of outer root sheath; *s*, developing sebaceous gland in early stage; *t*, cells degenerating to make way for the advancing hair.

and though involuntary in man is under the control of the will apparently in many animals.

Fig. 293 shows a section of one of the large tactile hairs of the cat, and it will be seen that there is a remarkable sinus between the layers of the dermic covering. The sinus contains blood and is traversed by a connective tissue network, the strands of which are covered by endothelial plates. The sebaceous glands are here rudimentary.

The hair-follicle develops as a downgrowth of epithelium from the surface into the connective tissue beneath—a downgrowth which becomes enlarged and invaginated at its lower extremity by the dermic papilla in much the same way as the enamel germ of the developing tooth. The epithelial cells immediately upon

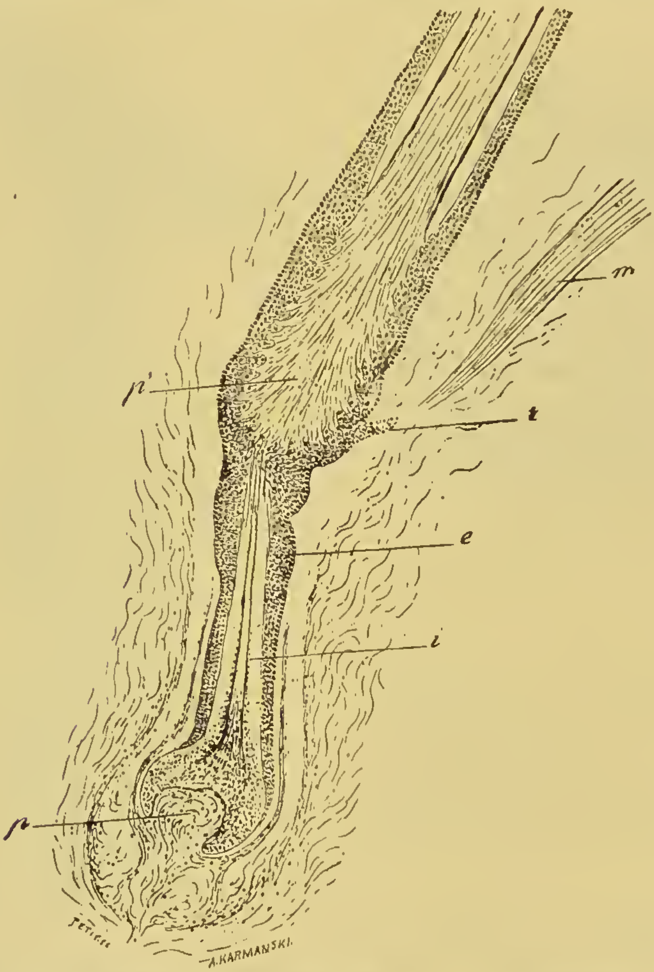

Fig. 295.—Hair being Shed and New Hair Developing to take its place.

p, Papilla; *i*, new hair growing upwards; *e*, outer root sheath; *p'*, degenerated base of old hair; *m*, erector pili muscle.

the papilla multiply and extend upwards, the others falling away to either side of them; the growing cells forming the hair and inner root sheath, while the displaced epithelium remains as the outer root sheath. The continued growth of the hair during life is due to proliferation of the cells above the papilla.

In leaving the hair-follicle, attention may be drawn to the fact that the secretion of sebaceous matter differs somewhat from the process of secretion by an ordinary gland. In the sebaceous gland the secreting cell perishes as such to form part of the secretion itself, and the continuance of the secretion depends on the appearance of another cell to take its place and in its turn be sacrificed. In the ordinary gland the cell discharges the secretion it has elaborated in its interior into the lumen of the alveolus, renewing its own substance at the same time to the end that it may repeat the same act of secretion when required. The secretion of milk, we shall see, may be regarded as a connecting link between the process of secretion by an ordinary and by a sebaceous gland.

The so-called "glandulæ ceruminosæ" of the external auditory meatus, although so named, according to some do not secrete the "wax" of the ear, but are merely sweat glands, the sebaceous glands of the hairs of the meatus secreting the fatty matters of which the wax is composed. This the sebaceous glands certainly do; but it seems also to be the fact that the ceruminous glands—the sweat glands of this region—do secrete matter of a fatty nature. They may also supply the pigment of the wax.

The *Meibomian glands* of the eyelids are the sebaceous glands of the large hair-follicles in this region, the *glands of Moll* being sweat glands.

Of the **functions of the skin**, one of the most obvious is that of *protection* of the body, and this is not merely mechanical but nervous, for it is one of the principal sense organs. With regard to the question of a *respiratory* function, there has been some difference of opinion. Animals, such as the frog, when the lungs are removed survive for some time, respiration going on through the skin. It is needless to say that this is not the case with man and mammals, and indeed in their case it is doubtful if any true cutaneous respiration is possible, on account of the thickness of the epidermis. It is true that when the body is enclosed in an air-tight chamber unconnected with the respiratory passages, the air in the chamber gains carbonic acid and loses oxygen, the gain of carbonic acid being said to amount to as much as 4 grms. daily. But the CO_2 may be derived from decomposition taking place in the sweat on the surface of the body, and the loss of oxygen may be due to the oxidation of the sweat constituents. A small animal, such as the rabbit, when coated with an impermeable varnish dies in a short time; but this is not due to the arrest of cutaneous respiration, which must

be small indeed, if it exists at all, nor to the reabsorption of the sweat constituents, but to the interference which is thus caused with the heat-regulating mechanism of the body. The part it plays in the *regulation of the temperature* is one of the main functions of the skin. When the rabbit is varnished the cutaneous vessels become dilated, there is an increased loss of heat, and the animal dies from cold, as it does if it be simply shaven. Another function of the skin which may be mentioned is that of *absorption*, though this, like its respiratory power, is at best insignificant. Under ordinary circumstances no absorption takes place from the skin unless the surface be abraded so as to expose the dermis, when absorption readily takes place. But even when the skin is intact, solid particles may find their way through the epidermis when they are rubbed into the skin, as in the case of the process of inunction with mercury ointment. In this chapter, however, we are concerned with none of the above functions, whether trivial or important, but rather with the skin as an organ of *excretion*. But it should be borne in mind, that though a large quantity of water leaves the body by the skin, and we must speak of the skin as an excretory organ, the *raison d'etre* of this secretion is not that the fluid would find difficulty in leaving the body by other channels or that it is a necessary accompaniment of the solids excreted in the sweat. The solids of the sweat are merely accidental to the secretion of the water, and as far as their excretion is concerned might be entirely neglected by the skin. The pouring out of this large quantity of water upon the surface of the body is concerned with the maintenance of the normal temperature, and in this connection we shall have occasion to refer to it again later on when "Animal Heat" is under consideration. Premising this, we may now, however, regard the skin as one of the excreting surfaces of the body and turn to the secretion by it of sweat.

Secretion of Sweat.

The amount of the perspiration varies a good deal in different animals, and also the parts in which the perspiration takes place. Thus the horse sweats profusely, the ox to a less extent. Cats and dogs sweat on the pads of the feet, the former more freely than the latter. Rats, rabbits, mice and goats are said not to sweat at all. The pig sweats at its snout. Man sweats over the skin surface generally but more readily from the palms of the hands and next from the soles of the feet. The sweat proper is secreted by the sweat glands, but will usually be mixed to a

varying extent with the sebaceous matter from the glands of the hair-follicles.

As long as the sweat is small in amount the water and volatile constituents evaporate at once, and this is known as *insensible perspiration.* When the secretion is more rapid, so that complete evaporation has no time to take place and drops accumulate on the surface of the skin, we have what is known as *sensible perspiration.* The proportion between the insensible and sensible perspiration (the rate of secretion remaining constant) will depend on the state of the surrounding atmosphere. If this be dry, warm and constantly moving, the perspiration is rapidly evaporated, and may remain insensible, whereas if the air be moist, cool and stationary, it may collect in drops as sensible perspiration. But the secretion may be too feeble to result in sensible perspiration, however cool, moist and stagnant the atmosphere may be, or, again, it may be sufficiently rapid to secure its presence as sensible perspiration, however dry, hot or mobile the air may be. And this is what we are often familiar with in hot weather, the stimulus to the sweat glands afforded by the temperature and muscular exercise being more than enough to counterbalance the greater tendency to evaporation. The secretion of sweat is also affected by the amount of fluid imbibed, the state of activity of the kidneys, by drugs, mental condition, &c.

The *amount of sweat* secreted daily varies so much under different conditions that no definite statement can very well be made; but, roughly speaking, as much water is lost by the skin daily as by the kidneys. But, as before mentioned, it should be borne in mind that the losses of water from these two surfaces vary inversely, *i.e.*, the more there is lost by the kidney the less by the skin, and *vice versa.* In other words, the skin and kidney are in this sense complementary to each other.

Chemical composition of sweat.—The sebum consists of fats (olein and palmitin), fatty acids, a small amount of proteid, and some unknown extractives. If the sweat be scanty, these constituents of the sebum influence its quality—when very profuse it may be taken as representing the secretion of the sweat glands alone, for the amount of the sebaceous secretion, as we should expect from the method of its production, remains fairly constant.

The sweat is a clear, colourless fluid, alkaline in reaction when pure. When acid, the acidity is due to the presence of fatty acids derived from decomposing sebum. It consists chiefly of *water*, with a small quantity of *solids* amounting to about 1 to 2 per cent. Its peculiar odour in different parts of the body is due to the presence of volatile fatty acids. The following substances are

found in it:—(1) Sodium chloride and other salts; (2) volatile fatty acids, such as formic, butyric and caproic; (3) neutral fats and cholesterin; and (4) albumin and urea, in traces.

The albumin is probably derived from the epithelial scales of the epidermis and sebaceous glands rather than from the sweat glands, and the presence of urea normally, even in traces, has been disputed. *In disease*, however, as in the anuria of cholera, urea may appear in the sweat to such an extent that on drying it is found crystallised on the skin. Sugar may be present in the sweat, as in diabetes; bile pigment in jaundice; uric acid and urates in gout; lactic acid in puerperal fever; albumin in acute rheumatism, &c. Certain substances, also, when taken internally reappear in the perspiration, such as benzoic, tartaric and succinic acids, potassium iodide, compounds of mercury, and arsenic.

Relation of the nervous system to sweat secretion.—When the body is exposed to warmth the cutaneous vessels dilate, the secretion of sweat is increased, and heat is lost. On the other hand, when the body is exposed to cold the vessels become contracted, thereby driving the blood into the interior, the secretion and consequent evaporation of sweat is arrested, and the heat of the body thus conserved. But we should be mistaken if we assumed that the dilatation of the vessels was the cause of the secretion of the sweat. It is rather an accompanying phenomenon favourable to the act of secretion, which is itself under the control of the nervous system. This conclusion is foreshadowed by the fact that profuse perspiration may take place when the skin is anæmic, as in the sweating of phthisis, during the death agony, in the crisis of various diseases, in hysteria, &c. Furthermore, there is experimental evidence of the direct control of the nervous system. Thus if the peripheral end of the cut sciatic nerve of a cat be stimulated, a copious secretion takes place on the pad of the corresponding leg. That this secretion is independent of increased vascularity is shown by the fact that it takes place even though the vessels are constricted by the stimulation. The secretion also takes place if the artery to the leg has been previously clamped or ligatured so as to remove the pad from the circulation entirely; indeed, secretion follows stimulation of the sciatic if the limb has even been previously amputated. If atropin be injected, no secretion follows the stimulation, though the vaso-motor nerves are not affected by the drug. A somewhat similar experiment may be employed to show that the secretion ordinarily brought about by an increased external temperature is effected through the nervous system, and not by the direct action of the temperature on the secreting cells.

The sciatic nerve is divided on one side in the cat, and the animal placed in a hot-air chamber. In this case it is found that though all four pads are exposed to the same temperature conditions, only those of the untouched limbs are covered with perspiration.

A venous condition of the blood, as in dyspnœa, also leads to an increased secretion of sweat, and here also the effect is produced through the central nervous system. If the sciatic nerve on one side in the cat be divided and dyspnœa induced, only the pads of the untouched limbs sweat, though the same blood has been circulating through them all. The venous blood evidently acts upon a sweat centre.

Stimulation of the central end of the cut sciatic also causes sweating of the pads of the other feet, the secretion here being obviously brought about by a reflex mechanism.

The number and position of the *sweat centres* in man is as yet largely a matter of speculation. There may be a general sweat centre in the medulla, with subsidiary centres in the spinal cord. In the cat there are two spinal centres—one for the fore-limbs in the lower cervical cord and one for the hind-limbs about the junction of the dorsal and lumbar cord. The secretory fibres for the fore-limb in the cat leave the cord in the anterior roots of the upper dorsal nerves, and passing by the white rami communicantes into the thoracic sympathetic, reach the ganglion stellatum. Leaving the ganglion stellatum as non-medullated fibres, they reach the brachial plexus, and thence pass in the median and ulnar nerves to the pads of the fore-feet. The fibres for the hind limb leave the cord in the anterior roots of the lower dorsal and upper lumbar nerves, pass thence by the rami communicantes into the sympathetic, and so reach the sciatic nerve, in which they are carried to the pads of the hind feet.

CHAPTER XIII.

METABOLISM.

HAVING considered the changes the foodstuffs undergo in the alimentary canal previous to their absorption either into the blood-stream or the lacteals and the excretion from the body of the waste products—urea, water and carbonic acid—we may now turn to the more difficult question of the changes which the food undergoes in its passage through the body under the heading of "metabolism." The whole story of metabolism is very far from being plain to us; we catch glimpses here and there of the changes the food is undergoing, and from these glimpses we must piece together a history as well as we can. At the outset it is apparent that a large proportion of the foodstuffs passes through the liver on its way into the general circulation, and, as we should expect, important metabolic changes take place in this organ. The metabolic function of the liver is indeed of greater consequence in one sense than its biliary one. It must, however, be borne in mind that comparatively unimportant as the bile may be *when produced* to the economy of the organism, its production (*i.e.*, the elimination of the waste products from which it is derived) is of supreme importance to the continuation of life. With a view to the better understanding of these metabolic changes we will turn aside for a moment to consider its structure.

Structure of the liver.—The liver is a compound tubular gland, the secretion from which passes into the intestine through the common bile duct at the same point as that of the pancreas. The arrangement of the blood-vessels in the gland is peculiar to it, and the gland tubules themselves are arranged in a characteristic manner.

The whole organ is surrounded with a fibrous investment, classically known as *Glisson's capsule*, which is continuous with the connective tissue surrounding the blood-vessels and duct of the gland as they enter it, and affording a supporting sheath to these branches in their internal ramifications.

If the surface of the liver be inspected with the naked eye it will be seen to be marked out into a number of polygonal areas of the size of a large pin's head, and these areas represent the lobules of which the organ is composed. When looked at more closely, the areas are seen to have a dark centre and a lighter periphery, the former being composed of the tubules of the lobule, while the latter, which serves merely to define the polygons, represents a system of connective tissue septa separating (in some animals more completely than in others) the lobules from each other and continuous with the general fibrous investment of the organ on the one hand and the prolongations of it along the vessels and ducts on the other.

The lobular arrangement thus reminds us of that in the lung, but the disposition of the tubules in a lobule of the liver is peculiar to the organ itself.

A lobule of the liver, as already stated, is polygonal in shape, and is made up chiefly of a number of gland tubules arranged in a radiate manner round the centre and opening at the periphery into their ducts. These ducts lie in the interlobular septa of connective tissue, which, as we have seen, constitute the lighter boundary to the dark central portion of the lobules when the surface of the liver is looked at with the naked eye.

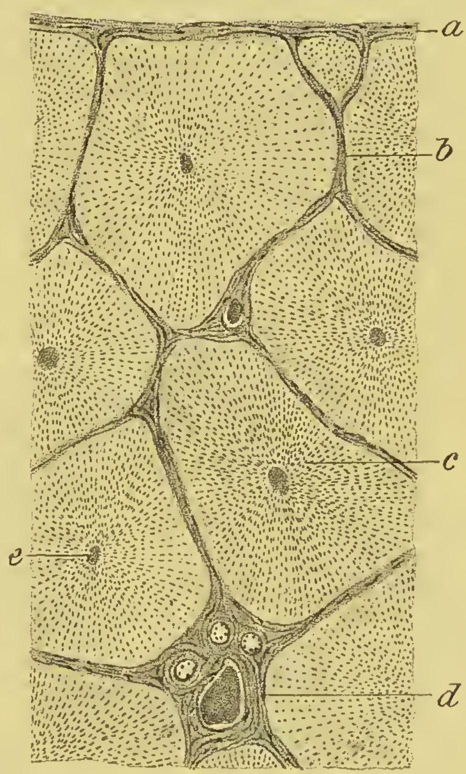

Fig. 296.—Section of Liver of Pig.

a, Glisson's capsule; *b*, trabeculæ separating the lobules; *c*, a lobule; *d*, portal tract, containing portal vein, hepatic artery and bile ducts; *e*, hepatic vein.

The blood from the alimentary canal passes to the liver in the portal vein, which, along with the hepatic vein (the efferent blood-vessel), the hepatic artery, and the bile duct, receives an investment or sheath from Glisson's capsule. Within the organ it divides again and again, its ultimate subdivisions lying, together

with those of the hepatic artery and bile duct, in the perilobular connective tissue. From this point, capillary branches are given off from the portal vein which pierce the lobules, and passing between the gland tubules reach their centre, where they open into the intralobular radicle of the hepatic vein. These intralobular radicles open in their turn into a larger vessel, the sublobular vein, and the various sublobular veins unite to form the larger branches of the hepatic vein itself. The walls of the branches of the hepatic vein contain no muscular fibres and the adventitia is very thin.

A lobule of the liver may thus be regarded as consisting of a radiating system of gland tubules, with a corresponding system of capillaries lying between them, and the gland tubules anastomose laterally with each other, as do also the capillaries. A very little adventitia containing lymphatic channels surrounds the latter, separating them from the gland tubules: indeed, the amount of connective tissue is so small that under an ordinary power of the microscope it is quite undiscernible.

A lobule is surrounded, wholly or partly, by the connective tissue which separates it from neighbouring lobules, and in this connective tissue are found branches of the portal vein supplying the capillary network between the tubules and the bile ducts which receive the secretion of the radially arranged gland tubules themselves. It will be observed that whereas the current of blood is from the periphery to the centre of the lobule, the current of secretion is from the centre to the periphery; but besides the portal vein and bile duct another vessel, the hepatic artery, is supported by the interlobular connective tissue. This vessel, much smaller than the portal or hepatic veins, corresponds to the bronchial artery of the lung, and supplies the connective tissue of the liver,

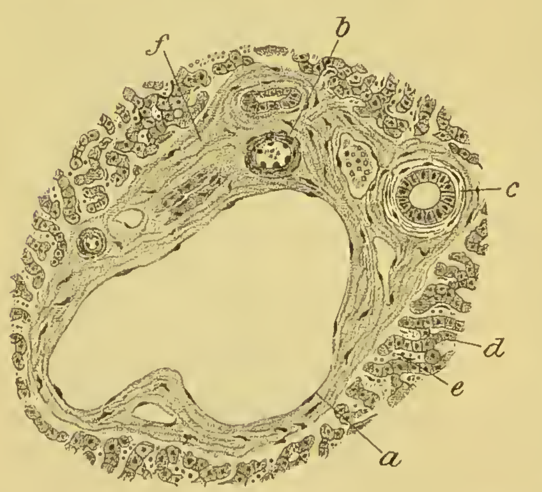

Fig. 297.—Transverse Section of Portal Tract of Liver of Child.

a, Portal vein; *b*, hepatic artery; *c*, bile duct; *d*, liver cells; *e*, capillaries between the tubules of the lobules; *f*, fibrous tissue of portal tract.

the vessel walls, &c. It empties itself ultimately into the smaller portal veins, and it may be also into the capillaries in the periphery of the lobules, *i.e.*, at the junction of the outer and middle thirds of the intertubular capillaries.

These vessels then—the portal vein and hepatic artery—together with the branches of the bile duct, lie in the interlobular connective tissue, but they are found more especially in the "nodes" of the fibrous network, where the connective tissue is naturally most in evidence. These nodal tracts of tissue are termed *portal tracts* or *spaces.* Such a tract in transverse section will vary in shape with the contour of the lobules between which it lies, and in size with that of the vessels, ducts, &c., it supports. These are represented by a branch of the portal vein (readily distinguishable from its large size and patency), a few sections of bile ducts and of the hepatic artery (very much smaller than that of the portal vein), and sections of lymphatic vessels and nerves.

Structure of the gland tubes.—The human liver, and indeed that of most mammals, represents a rather specialised form of the type as it occurs in the frog. Here the tubules are not arranged in the form of lobules, but are situated more diffusely throughout the gland network and alternating with a corresponding capillary one. The gland cells are large and wedge-shaped on section, the nucleus being placed in the outer broader part. The ducts are lined by columnar epithelium, whilst the intermediate portion connecting the gland tubules with the ducts has cubical cells.

As contrasted with the easily recognised character of the frog's liver, we find that of the mammalian comparatively obscure. The tubules in such a liver as that of the rabbit anastomose more freely, nor is their character, as tubules formed of cells surrounding a lumen, readily recognisable. We see, indeed, only a radiating series of anastomosing columns of polygonal nucleated cells, and these columns seem to terminate abruptly both towards the centre and the periphery of a lobule. There is no apparent connection (that is to say in an uninjected specimen) between the gland tubules and their ducts lying in the interlobular connective tissue. In reality, however, here, as in the frog, though not so easily made out, the tubules are connected with the radicles of the bile duct by a short intermediate ductule lined with low cubical cells.

Though in mammals the principle on which the liver is constructed (*i.e.*, that of an ordinary secreting gland) is not very apparent on microscopic examination, it must nevertheless not be lost sight of. It is in virtue of this that the bile "capillary" network and the blood-capillary network are invariably separated

from each other by at least a portion of a gland cell. The bile-capillary network represents the lumina of the anastomosing gland tubules, and is as much apart from the blood-stream as the lumina of the tubules of the salivary glands. In a specimen of the liver in which the portal vein has been injected with gelatine mass of one colour and the bile duct with that of another, two distinct networks are revealed—(1) a blood-capillary network comparatively large and coarse, and (2) a bile-capillary network which is infinitely finer. In such a section it will be noticed that whereas the larger transverse sections of the blood-capillaries are seen at the angles of the cells, the much smaller sections of bile-capillaries show as mere points in the middle of the adjacent sides of two gland cells: indeed, in the mammalian liver tubule, instead of several cells being arranged round a central lumen two cells alone surround it, their adjacent sides being grooved to form it.

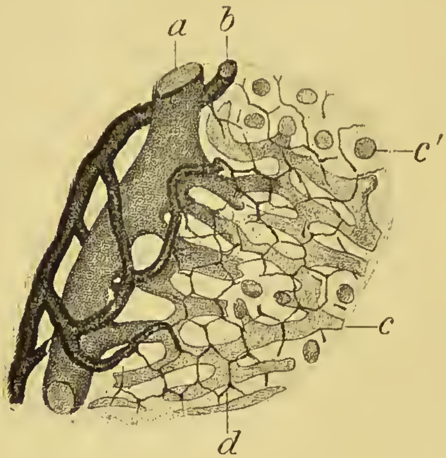

Fig. 298.—Section of Liver of Rabbit (Portal Vein and Bile Ducts Injected).

a, Portal vein; *b*, bile duct; *c*, portal capillary network; *c′*, capillary cut across; *d*, biliary network.

At the same time, the blood-stream is none the less effectively separated from that of the secretion of the gland by the intervention of the glandular epithelium. The difference between the liver tubule, in short, and that of another gland, such as the pancreas, lies in this, that in the former the lumen of the tubule lies between two cells, the opposing surfaces of which are grooved to admit of it, while in the pancreas and other similar glands four, five or more cells surround the lumen.

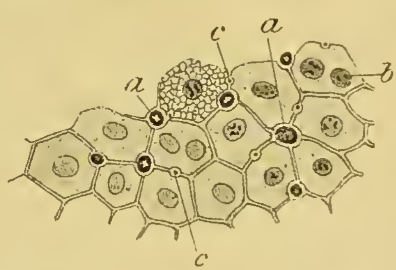

Fig. 299.—Section of Rabbit's Liver (Portal Vein and Bile Ducts Injected).

a, Blood capillaries cut transversely; *b*, nuclei of liver cells; *c*, bile "capillaries" cut transversely.

Moreover, the liver tubules anastomose with each other, and this is not the case with the tubules of other glands.

When we come to examine the cells themselves we find them polygonal in shape, with a round centrally-placed nucleus. The perinuclear protoplasm varies in appearance with the condition of the gland. In the resting condition it contains granules of glycogen, which disappear during activity—granules which are hyaline and stain a port-wine colour with iodine. They are found especially around the nucleus, and spread outwards through the cell protoplasm if the animal is supplied with a carbohydrate diet, disappearing from without inwards if it be fed on proteids alone.

Carbohydrate metabolism; Glycogenic function of the liver.—The dextrose absorbed from the alimentary canal passes in the blood of the portal vein to the liver, and is stored up in the hepatic cells for a time in the form of glycogen, to be given out gradually again as sugar, in conformity with the needs of the organism. This is the *glycogenic function* of the liver, whereby it acts as a storehouse for carbohydrate foodstuffs, and so prevents the organism being unnecessarily flooded with sugar after a meal or deprived of its due supply in the intervals between meals. We arrive at these conclusions from evidence of the following experiments:—

A rabbit is well supplied with carbohydrates (*e.g.*, carrots), subsequently killed, its liver quickly removed, chopped up and thrown into boiling acidulated water. After they have been boiled for a few minutes the pieces are rubbed up in a mortar with sand, again boiled in the same water as before, and the fluid filtered off. The filtrate is opalescent, often almost milky in appearance, and gives a port-wine colour on the addition of iodine, which disappears on heating and reappears on cooling. Sugar, tested for with Fehling's solution, is found to be absent from the solution or present in very small quantity. If, however, saliva be added to some of the opalescent fluid and the mixture be kept in a warm water bath the opalescence disappears, and on testing the clear fluid with Fehling's solution a considerable quantity of sugar is found to be present. The reaction with iodine is no longer obtained. The substance which has been converted to sugar is *glycogen* or *animal starch* and has the formula $C_6H_{10}O_5$. It may be precipitated as a white powder from the opalescent solution by the addition of alcohol until the mixture has an alcoholic strength of 60 per cent. The precipitate is then freed from proteid by boiling with alcoholic solution of potash, and then washed with alcohol and ether

and dried. Some of the characters of glycogen are given on page 17.

If, however, the liver in the preceding experiment be not removed immediately from the dead body, but allowed to remain *in situ* in a warm place for some hours, the filtrate obtained as before from boiling it in acidulated water shows little opalescence or none at all, and on testing with Fehling's solution it is found that a large quantity of sugar is present. Tested with iodine, either no port-wine reaction occurs or to a very much smaller extent than before. In fact, the glycogen present at death has been largely changed into sugar, and this has been brought about either by the action of some ferment which has not yet been isolated or by the activity of the liver cells themselves, agencies which would clearly be arrested by the process of boiling. The sugar formed is dextrose, however, as contrasted with maltose, the outcome of the action of most amylolytic ferments, such as those of the saliva, the pancreatic and intestinal juices, upon starch and glycogen, and this would lead us to suppose that it is probably the liver cells themselves that are concerned. The inference drawn from this experiment is that it virtually represents what takes place in the liver normally during life, the glycogen which has been stored up in the liver cells being gradually converted to dextrose and in that form served out to the organism. This is confirmed by the fact that in the intervals of digestion the blood of the hepatic vein contains more sugar than does that of the portal vein. On the other hand, during digestion, especially of a meal rich in carbohydrates, the blood of the portal vein contains more sugar than does that of the hepatic.

The amount of the glycogen found in the liver is very variable, and is markedly affected by the quantity and quality of the food supplied. Starvation leads to a rapid, followed by a slower, diminution of the hepatic glycogen, until only traces are left if the withholding of food be continued. If such a starved animal (rabbit) be given a meal of carbohydrates and killed after a few hours its liver will be found loaded with glycogen; but glycogen, though mainly derived from this source, may also have a proteid origin. Thus if a starving dog be fed on purified proteid (for meat itself contains carbohydrate), a much smaller amount of glycogen is found in the liver than after a carbohydrate meal, but at the same time it is distinctly in larger quantity than if the animal had been simply starved.

Fats appear to have no part in the formation of glycogen; an animal fed on fat is in the same position as far as hepatic glycogen is concerned as a starving animal.

Certain other conditions besides the supply of food affects the storage of hepatic glycogen. One of these is muscular exercise. The glycogen rapidly disappears from the liver of a fasting dog if it be made to undertake severe muscular work, much more rapidly than if it be starved alone. The glycogen, not only in the liver but also in the muscles, is apparently used up at once in the case of a sudden strain, such as that of starvation or muscular work, before the fat of the body has time to be affected; so that there may be no glycogen to be found in the liver in such cases while there is still plenty of fat in the tissues. The fat of the body seems to be reserved to meet a more continuous demand, while the proteid is drawn upon last of all in the final struggle. In frogs the temperature of the surrounding medium has a remarkable effect upon the storage of glycogen. Microscopically, glycogen is found in the cells of the liver in the form of a refractile hyaline material which becomes coloured a port-wine red with iodine. This material is soluble in water and may thus be dissolved out from its position, leaving vacuoles in the cell protoplasm. The liver cells of an animal after a meal rich in carbohydrates contain much of this material; those of a starved animal subsequently fed on proteid alone very little, and the cells are shrunken; after a merely fatty diet there may be none of it at all. The liver cells of a winter frog contain a great deal of this glycogen and are proportionately swollen, while in summer they contain little or none and are shrunken. This is the more remarkable as the winter frog is a fasting animal, while the summer frog is supplied with food. It seems to be due to the fact that in winter, when metabolism generally goes on slowly, sugar is produced in the body in excess of the requirements of the organism, and so is stored up in the liver; while in summer, when the metabolic processes go on more rapidly, all the sugar, whether produced in the organism itself or introduced from without, is used up as rapidly as it appears. The relation of the storage to temperature conditions in this case may be demonstrated by exposing a winter frog to a temperature of 20° or 25°C., when the glycogen rapidly disappears from the liver cells; whereas if a summer frog be cooled, glycogen commences to accumulate in the cells.

Glycogen is not only found in the liver but in the muscles, where it doubtless serves as a local depot of reserve material for providing muscular energy. It is also found in the placenta and very largely enters into the composition of embryonic muscle.

Though the liver thus acts as a storehouse of glycogen it does not necessarily follow that all the sugar reaching it from the alimentary canal is seized upon in the way that has been indicated.

Normally, human blood contains from ·05 per cent.* to ·15 per cent.* of dextrose, and some of the dextrose in the blood of the portal vein may pass directly through the portal circulation to maintain this percentage without undergoing the previous transformation to glycogen; but the amount so passing must be small, for if an excess of dextrose appears in the blood, and this may be readily secured experimentally by injection into the jugular vein of a rabbit, the surplus sugar is immediately excreted in the urine when the percentage in the blood rises above ·2.* A very much larger quantity of sugar, however, as we should expect, may be introduced into the portal vein without any appearing in the urine, in consequence of its arrest in the liver and storage there as glycogen; but if sufficient sugar be injected into the portal vein a temporary glycosuria may result, as it may indeed follow the ingestion of glucose or cane-sugar in sufficient amount. In such a case the explanation is that the liver has been so flooded as it were with sugar that the cells are unable to cope with the sudden demand made upon them, and sugar passes on directly into the general blood-stream in sufficient quantity to raise the percentage above ·2 and so secure its elimination by the kidney. Another example is thus afforded of the extraordinary selective power of the renal epithelium, which neglects the sugar in the plasma of the blood as long as it is present in normal quantity, but at once affords a passage to it when this quantity is exceeded.

The view we have thus outlined above that the liver acts as a storehouse for glycogen, which becomes converted during life either by a ferment or the activity of the liver cells themselves into sugar, and is paid out in this form through the blood of the hepatic vein to the tissues generally, is that originated by Claude Bernard and is the most generally accepted. According to Pavy, however, the blood of the hepatic vein in a fasting animal contains no more sugar than that of the portal vein, and he denies that the hepatic glycogen leaves the liver in this form. In other words, according to him, the postmortem conversion of glycogen to sugar, which we have already alluded to, is not a true picture of what occurs during life; and he believes that it is normally converted to some other substance or substances, thus forming a phase in the metabolism of fats or proteids. It is to be noted that there are great inherent sources of error in calculations based on quantitative estimations of the sugar of the blood of the hepatic vein, and it is the different results obtained in such analyses that have largely kept the

* These figures must only be regarded as approximate.

controversy alive. We cannot attempt to discuss the arguments here, but the weight of evidence generally seems to be greatly in favour of the older view of Bernard.

Fate of the carbohydrates of the food.—The dextrose leaving the liver is carried to all the tissues of the body, in which it undergoes oxidation to CO_2 and removal as this substance and water. This destruction takes place no doubt in all the active tissues, but more especially in muscle, leading to the production of energy in the form of heat and mechanical work. "The carbohydrate of the food directly increases the amount of CO_2 given off, and in proportion to the amount of such food taken" (Schäfer).

With regard to the question as to whether fats can be formed from carbohydrates, it is to be noted that in the fattening of animals by rearers it is a common experience that carbohydrates do produce fat—sheep and oxen fed on grass alone put on fat. Voit, however, considered that the carbohydrates of the food are not themselves transformed to fat, but produce their fattening effect by shielding the proteids from oxidation, the non-nitrogenous part of the proteid molecule being thus available for the production of fat. An important experiment by Lawes and Gilbert, however, disproves this explanation. Of two young pigs of the same litter, one was killed and the total amount of fat in its body determined. The other was fed for some weeks on proteid and an excess of carbohydrate, the exact amount of proteid supplied being noted. On killing the animal and estimating the fat in its body they found that the accession of fat during this time of feeding was greater than could be accounted for by the proteids of the food; for, assuming that the whole of the non-nitrogenous portion had been converted to fat, this would only account for two-thirds of the fat which had been formed, and some of the fat must therefore have been derived from the carbohydrates. This experiment, therefore, conclusively shows that under certain conditions of diet the carbohydrates of the food may to some extent be converted to fat. The transformation need not be, however, direct; the carbohydrate molecule may be split up into simpler compounds, and these again built up into fat.

Glycosuria—diabetes.—In the disease known as *diabetes mellitus* sugar accumulates in the blood and is excreted by the kidney in the urine. A similar result, so far as the excretion of sugar by the kidney is concerned, may be obtained temporarily in various ways. If the floor of the fourth ventricle of a well fed rabbit be punctured in the region of the vaso-motor centre, the animal excretes sugar in its urine for the next day or two, after which the urine again becomes normal; but if the rabbit, instead of

being well fed, be starved, so that its liver contains little or no glycogen, the puncture will not have the same effect, and we may conclude from this that the sugar in the first experiment was derived from the glycogen of the liver. The precise *modus operandi* of the nervous system in bringing about the result it does is not, however, clear. It may be due to a disturbance of the hepatic circulation affecting especially the hepatic artery, or it may be due to an interference with the action of nerves to the liver cells themselves. The liver is supplied by the hepatic plexus, which is an extension of the solar plexus, and receives fibres from both vagi and the abdominal splanchnic nerves. Division of the vagi does not produce diabetes, and glycosuria is caused by the puncture though both vagi have been divided. Similarly, division of the splanchnics on both sides does not cause diabetes, but puncture-diabetes is said not to result if the splanchnic nerves are previously divided or the cord cut above the level of the third or fourth dorsal vertebræ. It seems likely that the puncture acts in some way through stimulating the vaso-motor centre, for prolonged stimulation of many sensory nerves, *e.g.*, the sciatic, which affects the vaso-motor centre, may result in the production of temporary glycosuria. But we need not discuss this obscure matter further; it is enough for our purpose to note that the glycosuria following the diabetic puncture is due to the hurrying forward of the change to sugar of the hepatic glycogen, whereby an increased amount is passed into the hepatic blood, resulting in its excretion by the kidney, when the percentage in the blood generally exceeds a certain low limit.

A temporary glycosuria may also be produced artificially by other means, such as the administration of strychnia, curara, phosphorus, and carbon-monoxide, some of which may act by affecting the hepatic circulation, others directly on the hepatic cells.

The production of diabetes by the administration of the drug *phloridzin* is of special interest from the light it throws on carbohydrate metabolism. We have seen that glycogen can be formed in the body from proteids, presumably by a process of synthesis preceded by a splitting up of the proteid molecule, dextrose representing a stage in the synthesis. Phloridzin is a glucoside, but its effect in producing diabetes must not be attributed to this, as the amount of sugar excreted is much greater than could be thus accounted for, and, moreover, the same result is secured by the administration of *phloretin*, a non-glucoside derivable from it. The first effect of a dose of the drug is an excretion of sugar and an accompanying diminution of the hepatic glycogen, but the

remarkable result ultimately obtained is that sugar is still excreted in quantity on repeating the doses, even after all the store of glycogen has been removed from the body. Similarly, if the glycogen has been previously got rid of by starvation and muscular exercise, glycosuria still follows exhibition of the drug. The sugar must then be derived from the metabolism of proteid, and of this there is the additional evidence that the nitrogenous excretion—the urea—runs parallel with the saccharine; for, as we know, in the production of urea a considerable quantity of a carbon containing radicle is thrown off by the proteid molecule.

The diabetes then induced by phloridzin affords another instance of the production of sugar from proteids within the body; but there is another fact in connection with it which deserves notice. After the injection of phloridzin, the sugar in the blood, so far from being increased in amount, is found to be actually diminished, and this is quite a different state of affairs to what we find in the case of diabetic puncture, when sugar is excreted because the percentage of it in the blood rises above a certain limit. It has been suggested that the diabetes of phloridzin is the result of an interference by the drug with the further synthesis of dextrose into glycogen, after its production from body proteids. We may suppose that normally a certain amount of dextrose is produced from proteid, some of which may pass into the blood-stream directly, while the rest is synthetised into glycogen and stored up in this form. An interference with this further synthesis would lead to an accumulation of sugar in the blood-stream and its excretion by the kidney; but such an explanation is merely conjectural and can scarcely be reconciled with the diminution of sugar in the blood which is characteristic of this form of glycosuria, and, moreover, if the renal vessels be tied no accumulation of sugar in the blood follows the administration of phloridzin. This at once suggests that the kidney epithelium may be rendered permeable to sugar by the phloridzin, and this is confirmed by the fact that if the drug be injected into the renal artery, the same kidney begins at once to excrete sugar, to be followed by the other kidney after a short interval. The result of this action on the kidney can easily be followed out. The normal percentage of sugar in the blood will fall; the store of glycogen in the liver will be drawn upon to maintain the falling percentage as long as any remains; the proteids will then be attacked, resulting, as we have seen, in an increase in the excretion of urea, which will run parallel with that of the sugar. The precise way in which the phloridzin produces its effect on the kidney is not quite clear, but it has been suggested by Minkowski

that it becomes split up in the kidney into phloretin and sugar, the latter being eliminated, while the former combines with the sugar of the blood to again form phloridzin, which is again split up as before.

We may now turn for a moment to the consideration of the disease known as *diabetes mellitus*, which we merely mentioned at the commencement of this section. Here there is an accumulation of sugar in the blood sufficient sometimes to raise its percentage to from ·4 to ·6. It may be that in some of the more tractable forms of the disease the increase of sugar in the blood is due to a failure on the part of the liver to store up the sugar of the food as glycogen, resulting in its immediate projection into the general circulation and consequent excretion by the kidney when the resultant rise in the percentage present in the blood has taken place. The ordinary method of treatment in such a case of restricting the carbohydrates taken as food may be successful; but in many severe cases of diabetes, in which the diet has been strictly limited to proteids and fats, it has been found after death that the liver contained a large quantity of glycogen, so that in these cases the glycogenic function of the liver was not apparently in abeyance. We may suppose that in some way sugar has ceased to be a food for the tissues—that they are unable to make use either of the sugar taken as food or that split off from the proteids of the body when sugar is withheld, and that sugar therefore accumulates in the blood and is excreted by the kidneys.

The presence of glycogen in the liver when carbohydrates have been withheld might seem at first sight to indicate that hepatic glycogen was the result of metabolism of the liver cells stimulated by the proteid food; but, on the other hand, as we know, sugar may be formed in the muscles as the result of the splitting off of the carbon-containing radicle when proteid matter is broken down to yield urea, and the glycogen in the liver may thus have its precursor in sugar produced in the body elsewhere and brought to it by the portal vein though no carbohydrates are given as food.

In severe cases of diabetes other abnormal products of metabolism arising from the incomplete combustion of proteids appear in the urine, such as acetone, aceto-acetic acid and oxybutyric acid; and it may be that the coma which often precedes a fatal termination is caused by the union of such substances with the alkalies of the blood and its consequent impairment as a carrier of CO_2.

Why the tissues should be unable to make use of the sugar. as has been suggested, we are unable at present to explain. It

has been surmised that perhaps normally the sugar may require previous elaboration in other organs, and that it is for lack of this, through disease of such organs, that it becomes useless to the organism, and indeed hurtful to it. In many fatal cases of diabetes the pancreas has been found diseased, and there is experimental evidence that the gland is intimately concerned with the metabolism of sugar. If the pancreas of a dog be removed, the animal acquires severe diabetes, which continues even if the animal be starved or fed on a purely proteid diet, and invariably proves fatal. Here, as in severe human diabetes, the excretion of urea runs parallel with that of the sugar, showing that the latter is derived from the breaking down of proteids, and acetone, aceto-acetic acid and oxybutyric acid make their appearance in the urine. It seems to be necessary to remove the whole pancreas; if some of it be left diabetes does not occur, nor does it ensue if a portion of the gland be transplanted, *e.g.*, beneath the skin or in the peritoneal cavity, nor does ligature of the duct of the pancreas cause it, so that, apparently, diabetes is not due to abolition of the secretion. How the pancreas affects the metabolism of sugar we are at present unable to say. The amount of sugar in the blood rises immediately after complete removal, and the condition therefore resembles puncture diabetes, as contrasted with that induced by phloridzin, in which the amount of sugar in the blood is certainly not increased. The pancreas may act upon the dextrose brought to it in the blood, or it may give rise to some "internal secretion" which passes to the blood and tissues. The glycosuria is not removed by giving raw pancreas by the mouth, as contrasted with the relief obtained in cases of thyroidectomy by administration of the gland itself.

We cannot, however, continue the subject further here. It is to be admitted that the pathology of diabetes in its various forms is still very obscure, as it must necessarily be in the present state of our knowledge of metabolic processes generally. "Que sais-je?"—the motto of Montaigne—must also be ours in dealing with most of the problems of metabolism.

Metabolism of proteids.—We have seen that the carbohydrates of the food are carried to the liver as dextrose in the blood of the portal vein; and, similarly, the products of absorption and assimilation of proteid food pass to the same organ by the same path. We should thus suppose *a priori* that the influence of the liver on proteid metabolism would be great, and when we inquire into the matter further, as we shall immediately, we shall find that this is the case. We shall follow out the course of the proteids after absorption into the blood-stream as we did that

of the carbohydrates, but before doing so it may be well to allude shortly to the different views which have been held as to the ultimate metabolism of proteids in the tissues generally.

Voit distinguishes two kinds of proteids—the *tissue-proteids*, which form an actual part of the living substance and which we may speak of as *protoplasm*, or perhaps better as *bioplasm*, and the *circulating proteids*, which occur in the blood and in the interstices of the bioplasm without forming a part of the tissue itself. Starting from this basis, two extreme views have been put forward as to the manner in which the proteids of the body are metabolised. One of these is that the circulating proteid before it can be split up and oxidised becomes built up into tissue itself, *i.e.*, becomes an integral part of the bioplasm. Thus in a tissue cell we may suppose that, on the one hand, molecules of dead proteid, derived as circulating proteid from the blood, are seized upon and fresh molecules of bioplasm formed (anabolism), while, on the other, previous living molecules of the same cell are split up and fall to pieces (katabolism). This was the view of Liebig, that only tissue proteids undergo metabolism—that before the circulating proteids can be metabolised they must undergo the transformation to tissue proteids or bioplasm. The other view—that of Voit—is that the circulating proteids can be split up and oxidised outside the actual molecules of the bioplasm, but as the result of contact with them. According to this view, tissue proteid as such does not undergo metabolism, but must first (*e.g.*, in inanition) be dissolved up and carried in the blood-stream as circulating proteid to other tissues, in which it becomes split up and oxidised. Certain experiments were carried out by Schöndorff which seem to favour strongly the theory that the proteids carried to the tissue become incorporated in the protoplasm of the cells. If blood taken from a well-fed animal, and therefore rich in proteid, be passed first through the vessels of the hind limbs and then through the liver of a starved animal, the amount of urea formed was very small indeed; whilst if the perfused blood was taken from a starving animal, and therefore poor in proteid, and passed through the limbs and liver of a well-fed dog, the amount of urea was increased. If Voit's theory were correct, the quantity of urea in the first case would have been large, and in the second small, in accordance with the amount of proteid in the circulating fluid. We cannot here discuss the arguments for and against these views, although it has seemed desirable to state them at this juncture; and we can but say in leaving the matter that many considerations lead to the conclusion that both views go too far, and that it is more reasonable to suppose that

metabolism may occur as a splitting up and oxidation both of the molecules of the bioplasm and of the circulating proteids or non-proteid matter in contact with the bioplasm.

We may now return to trace the course of the proteids from the alimentary canal. We have seen, in considering digestion, that the proteids of the food are converted by the secretions poured out upon it to albumoses and peptones, and ultimately probably entirely to peptone. They do not, however, enter the blood-stream in this form, but are again reconverted to proteid in their passage through the wall of the alimentary canal, the columnar epithelium being probably the active agent in the conversion. Furthermore, it is to be borne in mind that some of the proteid of the food may be carried beyond the peptone stage, leading to the formation of amido-acids (see "Pancreatic Digestion"). These amido-acids, *e.g.*, leucin, will enter the portal blood-stream with the proteids, and it is probable that in the liver they are converted by synthesis to urea, for the administration of amido-acids, or their addition to the blood circulating through the liver, leads to an increase in the urea leaving that gland and an increase in the urea excreted by the kidneys. However, this method of the formation of urea from proteid need not detain us here, as it can occur to but a small extent normally, and in so far as it does occur merely signifies a loss of so much proteid food to the organism.

The blood of the portal vein, then, will contain the food proteids transformed from peptones into serum-albumin and serum-globulin, the extractives of meat, and such substances as the amido-acids derived from the further decomposition of peptones in the alimentary canal; and though these additions to the ordinary constituents of the blood may not be revealed by direct analysis, the difference between the portal blood collected during digestion and in the intervals between may readily be demonstrated physiologically. If blood collected from the portal vein during the absorption of proteid from the intestine be passed through the liver, it shows an increase of urea, whereas blood taken in the intervals of absorption and similarly treated shows no such increase. Having traced the proteids of the food thus far, we may now inquire what fate may befall them in the liver itself.

Influence of the liver on proteid metabolism.—We saw that the liver acted as a storehouse for the sugar, or at least a great part of it, reaching it in the blood of the portal vein, the sugar being converted to glycogen; and we may now inquire if any corresponding storage of proteid material takes place. Broadly speaking, it

does not. For the most part the proteid derived from a meal passes through the liver unchanged, and we must look for its place of storage in the tissues beyond. But we have already seen that under certain circumstances, *e.g.*, when a starving dog is fed on purified proteid, a certain amount of glycogen appears in the liver, and here it seems probable that the proteid molecule has been so split up that one part of it becomes urea or an antecedent of it, while the other, after undergoing further changes and synthesis, remains as glycogen. This need not, however, take place in the case of an animal with a mixed diet, in which the carbohydrates present would be enough to account for the glycogen formed. It is, indeed, merely an instance of the proteids being attacked when there is a failure in the carbohydrate supply. Similarly, also, in the case of the fat globules frequently observed in the liver cells, especially during absorption. When this fat appears in the liver after a mixed meal containing fats, we may suppose it to be derived from the fats of the food after they have entered the general circulation through the thoracic duct; but in the absence of fat in the food, the fat in the hepatic cells may be derived from the food proteids after their decomposition to form urea. Of course, in both these cases of glycogen and fat formation the splitting up of the proteid molecule might have occurred elsewhere, but there is no reason to think that the liver has not the same power of splitting the proteid molecule in this way that other tissues have.

We may now proceed to consider the influence of the liver upon metabolism apart from any power of storage it may possess of food proteids or their derivatives, which we have seen to be small in amount and probably only exercised under exceptional circumstances. In the first place, we must recognise that urea and uric acid are produced probably entirely, but certainly mainly in the liver. Urea in mammals and uric acid in birds are found in larger proportion in the liver than elsewhere. We have also seen that when blood containing the absorbed products of proteid digestion is perfused through the liver it shows an increase in urea; and a similar increase in urea appears in blood to which ammonia compounds, such as carbonate of ammonia, have been added previous to perfusion; but we shall return to the evidence of the formation of urea in the liver immediately.

We must not conclude, however, that because urea, the chief ultimate product of proteid metabolism, is formed in the liver that the food proteids of the portal blood are split up in the liver to form urea. This must occur to an entirely unimportant extent only, for in such a way the whole of the proteids of the

food would be absolutely wasted and lost to the organism generally, just as the small moiety which becomes split up beyond the peptone stage in the alimentary canal is lost to the tissues. What really takes place is that the greater part of the food proteids which reach the liver passes through it into the general circulation without undergoing any change and is distributed to the tissues generally. It is to be noted, however, that even after absorption of a large amount of proteid, the proteid in the general blood and lymph stream is not increased in amount to any material extent, and the absorbed proteid is therefore presumably stored in some of the tissues of the body, chief amongst which we should suppose to be the muscles, and this is confirmed by the fact that the metabolism of the muscles is increased by an increase in the absorbed proteids in the blood, and as the increased metabolism of the muscles lasts some time it is to be presumed that the surplus proteid is at first stored within them. According to Voit, as we have seen, the food proteid does not become built up into the muscle bioplasm but is merely brought into contact with it by being received into the interstices between its molecules; this contact stimulating the bioplasm to activity and so inducing metabolism in the circulating proteid. On the other hand, according to the view of Liebig, which has been supported by Pflüger, the food proteid is stored by being directly built up into the muscular bioplasm, which is at the same time stimulated by this increased growth to increased destruction. This we may illustrate thus: If we imagine a piece of tubing to be filled with a row of marbles, then on pressing another marble in at one end, the marble immediately at the other end will fall out to make room for the new comer; and so also with two, three or more marbles. Thus the greater the amount of food proteid brought to the muscle the greater the destruction of the old bioplasm to make way for the new bioplasm which is built out of the food proteid. As we have already indicated, the truth may lie somewhere between these views. Foster, speaking of muscle as an instance of a tissue, says—"Both framework and intercalated material undergo metabolism and have in different degrees their anabolic and katabolic changes; both are concerned with the life of the organism, but one more directly than the other." Voit's view has not, on the whole, found favour with physiologists, who incline for the most part towards Pflüger's.

Be this as it may, whether the food proteid is built up into the muscle bioplasm or is merely stored in its interstices, its storage is not for long, for in a few hours the whole of the absorbed proteid is got rid of in the form of urea.

We do not find, however, that the muscles themselves contain urea, or only in very small amount, so that the final stage of proteid metabolism must take place elsewhere. The transformation of proteid to urea is no doubt accomplished in several stages, the first of these taking place in the muscles principally and the last, as we shall see, in the liver; and we have now to inquire what precursor of urea may be formed in the muscles from the food proteids brought to them and either built up into their bioplasm or lodged within it as intercalated material. It is when we come to deal with questions such as these that the gaps in the history of metabolism become evident; we cease to be on certain ground and have to rely largely on processes of deduction.

Creatin is normally found in considerable quantity in the analysis of dead muscle, and it is, moreover, capable of conversion in the laboratory to urea and sarcosin. We might therefore be inclined to suppose that creatin is produced in the muscle as the chief antecedent of urea, and is split up elsewhere in the body to urea and sarcosin, the latter of which undergoes further changes and is itself converted to urea. A difficulty arises, however, in our acceptance of this view, for if creatin be injected into the blood-stream or administered as food it appears in the urine as creatinin and not as urea. It is quite clear, therefore, that we cannot in the face of this observation suppose that creatin, whether a precursor of urea or not, leaves the muscles in that form and is split up elsewhere (*e.g.*, in the liver) to form urea; for if this were the case why should not the creatin injected into the blood-stream share the same fate?

The precursor of urea, therefore, for which we are looking, even if derived from the creatin of muscle, as is very possible, must leave the muscle in some other form, and there seems considerable reason for supposing that certain ammonia compounds are to be regarded as the antecedents we are in search of. Thus if the blood of a fasting animal be perfused through the limbs of a well-fed one, it acquires an increase of ammonia salts; and, again, when ammonium chloride is administered to a dog there is an increase in the urea of the urine corresponding to a large portion of the nitrogen of the salt. It is probable that the ammoniacal bases thus formed from the proteid break down, combine with the acids present in the tissue, forming salts such as the lactate, carbonate and carbamate of ammonia, which are then carried in the blood-stream to the liver and there converted into urea in mammals and uric acid in birds.

Thus we may assume that the proteid molecule in muscle (whether creatin be an intermediate stage or not) becomes split

up into a nitrogenous portion, which leaves the muscle as the precursor of urea, and a non-nitrogenous portion. As for the fate of this latter we know very little certainly except that ultimately it becomes oxidised to carbon dioxide and water. As glycogen is constantly found in muscle, it may be that some of the non-nitrogenous portion of the proteid molecule undergoes this conversion and is also converted to sugar. This is supported by what we have already seen of the production of sugar in cases of severe diabetes when all carbohydrates are withheld, and similarly also in cases of phloridzin poisoning. The sulphur of the proteid molecule evidently becomes oxidised to form sulphates, for the excretion of sulphates runs parallel with the proteid metabolism.

Formation of urea in the liver.—Nitrogenous metabolism occurs in all the tissues, but principally in the muscles, and the ultimate product of this metabolism is urea; but, as we have seen, no urea is found in muscle, and the final stage in the production of urea cannot take place there. The liver, however, contains a relatively large amount of urea, and we have reason to regard it as the organ in which the nitrogenous products of previous stages of proteid metabolism are converted to urea. The argument is as follows:—

1. If blood containing ammonium carbonate, or carbamate, or lactate be perfused through the surviving liver of a well-fed animal, it shows an increase in urea, just as ammonium salts taken internally lead to an increase in the urea excreted. Similar blood perfused through the limbs of a dog shows no increase of urea. From these experiments we conclude that it is in the liver and not in the muscles that synthesis of ammonia compounds and urea takes place.

The following may represent the change which takes place when carbonate of ammonia is converted to urea, the carbamate being the immediate precursor:—

$$\begin{array}{ccccc} \begin{array}{l} \quad O\,(NH_4) \\ C = O \\ \quad O\,(NH_4) \end{array} & - & \begin{array}{c} H_2O \\ \text{(Water)} \end{array} & = & \begin{array}{l} \quad NH_2 \\ C = O \\ \quad O\,(NH_4) \end{array} \\ \text{(Carbonate of ammonia).} & & & & \text{(Carbamate of ammonia).} \end{array}$$

$$\begin{array}{ccccc} \begin{array}{l} \quad NH_2 \\ C = O \\ \quad O\,(NH_4) \end{array} & - & \begin{array}{c} H_2O \\ \text{(Water)} \end{array} & = & \begin{array}{l} \quad NH_2 \\ C = O \\ \quad NH_2 \end{array} \\ \text{(Carbamate of ammonia).} & & & & \text{(Urea).} \end{array}$$

2. The experiment in which the blood of a dog containing the products of digestion is perfused through an excised liver is also suggestive. It shows an increase in urea, which cannot be

supposed to be merely washed out from the liver, as the blood of a fasting dog has not the same effect. The active substances in the blood which produce the effect may be amido-acids from the intestine, such as leucin, which, as we have seen, is one of the results of the further splitting of peptones in the intestine, or the products of increased metabolism in the tissues as a result of the food supplied to them, or both of these, but chiefly the latter.

3. When the liver is removed in mammals, the portal vein being connected with the inferior vena cava by an Eck's fistula, so as to avoid congestion of the intestinal circulation, the urea excreted is largely diminished, its place being taken by carbonate and lactate of ammonia. The inference here clearly is that the ammonia salts, which form a stage in the metabolism of proteids, in the absence of the liver are no longer converted to urea in that organ, and hence are excreted as they are by the kidney. On the other hand, when carbonate of ammonia is administered to a mammal under normal conditions the ammonia is not increased in the urine, but an amount of urea is excreted in proportion to the amount of the salt given.

4. In cirrhosis of the liver the urea excreted is also diminished, and its place taken by ammonia compounds. The same occurs in acute yellow atrophy of the liver, and here leucin and tyrosin are also found in the urine. These latter, however, may be derived from the intestine and not from tissue metabolism.

5. In birds, uric acid replaces urea as the final product of proteid metabolism, and it can be shown that in geese uric acid is formed in the liver. In these birds there is a communication between the portal vein and the vena advehens of the kidney, and this enables the portal vein to be ligatured or the liver removed without producing the stasis which follows in mammals (Minkowski). When the portal vein in geese was ligatured, the uric acid in the urine fell from representing 60 to 70 per cent. of the total nitrogen excreted normally to 3 to 6 per cent.; while the ammonia in the form of lactate increased from 9 to 18 per cent. to 50 to 60 per cent. The lactate of ammonia represented fully half the solids of the urine, though none is present under ordinary conditions. The amount of urea excreted was unaltered; if injected into the blood or stomach it was excreted as such in the urine, whereas in the normal animal it is converted to uric acid. From the above evidence we therefore conclude that the final transformation of the product of proteid metabolism in the tissues generally to urea takes place in the liver under the influence of the hepatic cells; but we must be on our guard

against inferring that no such transformation occurs elsewhere. Urea still continues to be formed and excreted in the urine to some extent after complete removal of the liver, though it is largely replaced by ammonia salts. Probably other glandular organs, such as the spleen and lymphatic and secreting glands, have their share in the formation of urea.

Urea formation does not occur to any great extent in the kidney. When the kidneys of a dog are removed, urea accumulates in the blood and tissues, while the animal remains alive, to about the extent to which it would under normal circumstances have been excreted in the urine. Again, if blood containing carbonate of ammonia be perfused through the kidney it shows no increase in urea, in this way contrasting with similar blood perfused through the liver. By these experiments we may exclude the kidney as the organ concerned in the final stage of urea formation. Of course this is not to say that nitrogenous metabolism does not take place there. The proteids of the kidney break down and contribute their quota to the sum of the antecedents of urea in the blood in the same way that those of any other tissue do. All these experiments are intended to show that the final synthesis to urea of proteid metabolites is not accomplished in the kidney. At one time the contrary view was held, and the power of the kidney to form hippuric acid from benzoic acid and glycin might certainly at first sight lend colour to the older doctrine.

Uric acid, like urea, is not to any appreciable extent formed in the kidneys but is merely withdrawn by them from the blood. In birds, in which it forms the chief end product of proteid metabolism, it can be detected in the blood, and if the liver be extirpated lactic acid and ammonia appear in the urine. These substances are probably formed in the muscles, as in mammals, and the final conversion to uric acid takes place in the liver, just as the final conversion to urea in mammals takes place in that organ.

But the uric acid of mammalian urine has not quite the same history as the urea. It appears to be derived from the disintegration of the nucleo-proteids of the food or tissues (spleen, lymph-glands); such disintegration resulting in the formation of xanthin bases, which partly undergo further oxidation and are excreted as xanthin, hypoxanthin and uric acid by the kidney *before they reach the liver*, for if uric acid itself be administered to dogs the urea and not the uric acid of the urine is increased, the transformation taking place in the liver. As bearing upon this difference in the history of the uric acid of mammalian urine, it may be pointed out that the administration of amido-acids or ammonia salts leads to no increase in its

amount, nor is this necessarily increased by an increase in the quantity of proteid ingested. On the other hand, the administration of organs rich in nucleo-proteids, such as the thymus, seems to be most conducive to an increase in the uric acid production. A similar increase is also observable in diseases such as leucocythemia, in which there is an increased formation and destruction of lymph-cells.

Effect of muscular exercise on proteid metabolism; source of muscular energy.—It was held by Liebig and the older writers that the energy of muscular contraction was supplied by proteids—that the proteids alone were devoted to the building up of the muscles and proteid tissues generally, and that muscular energy was the result of their oxidation alone, while the heat of the body was produced by the oxidation of the carbohydrates and fats. Now, if it were the fact that muscular energy was derived exclusively from the metabolism of the proteid constituents of muscle, we should expect to find that the excretion of urea would be increased by muscular work; but many observations have been made which show that this is not so, the most notable perhaps being those of Fick and Wislicenus. These observers ascended the Faulhorn mountain on a non-nitrogenous diet, and found that the urea excreted was totally inadequate to account for the amount of energy expended, for whereas the work done amounted to roughly 130,000 and 150,000 kilogram-metres in the two cases respectively, the energy represented by the proteid metabolism (corresponding with the nitrogenous excretion) was only equal in each case to 68,000 kilogram-metres. It is to be borne in mind, too, that the cardiac and respiratory energy expended is not counted in here with the work done, which makes the real discrepancy greater. We can only conclude that the energy set free was at least partly derived from other sources than proteid metabolism—that it resulted from the oxidation of non-proteid matter—and the increase in the output of CO_2, which is found to take place in proportion to the amount of exercise, points in the same direction. These experiments, therefore, led physiologists to rush to the opposite extreme, and to conclude that muscular energy is derived entirely from the oxidation of carbohydrates and fats and that proteids have nothing at all to do with it. Neither of these extreme views, however, can now be said to hold the field, the tendency being to modify both. It has been found by Pflüger and his disciples that in experiments similar to those of Fick and Wislicenus a marked increase of proteid metabolism, as shown by the excretion of nitrogen, took place, and though this may very

well have been due to a deficiency in the supply of non-proteid matter leading to the proteids being made use of instead, it undoubtedly shows that muscular energy can be evolved from the oxidation of proteids. Again, a dog fed on lean meat can undertake prolonged muscular work far in excess of what can be accounted for by the carbohydrate and fat it obtains from its food or tissues. It is a common experience, too, that athletes are largely trained on a meat diet; but, on the other hand, it must be noted that an enormous amount of muscular work is accomplished by the natives of some countries on a diet consisting almost entirely of carbohydrates. These two opposing instances may well be taken to show the rashness of drawing partisan conclusions from such data in a hurry.

But even granting that under certain circumstances of diet or over labour there is an increase in the nitrogen excreted, indicating the proteids as the source of muscular energy, or of some of it, in these cases, it must be allowed that it remains a fact that under ordinary conditions the chief effect upon excretion of muscular exercise is an increase in the amount of CO_2 given off, without any increase in the excretion of nitrogen, or so small a one as to be of little meaning, and we may practically regard it as a law of nitrogenous metabolism that under normal conditions it is independent of muscular work (Stewart). Thus in a normally nourished animal with a sufficiency of non-proteids these are the chief sources of muscular energy; when they fail the proteids will be drawn upon. "The most probable view appears to be that muscle, like other cells, although it can only actually build up its bioplasm out of proteid, is nevertheless able to produce muscular energy by oxidation—perhaps occurring outside the actual molecules of its bioplasm, but under their direct influence —of any or all the organic foodstuffs, and that this process is attended only by such small disintegration and loss of the proteid material of the bioplasm as is necessarily attendant upon its functional activity—a loss which is comparable to the wear and tear of the working parts of the machine as distinct from its consumption of food" (Schäfer).

The **metabolism of fat.**—We have already had occasion to consider the histological features of a fat cell and its development, but it may be expedient to recall these shortly here. When fat is to be formed, connective tissue corpuscles begin to exhibit in the midst of their perinuclear protoplasm a gradually increasing number of small droplets of fat, the cell protoplasm at the same time increasing in bulk. As the development of a fat cell proceeds

the droplets increase in size and coalesce with each other to form larger droplets, which in their turn run together, until there is a single large globule of oil surrounded by the cell envelope. The nucleus of the cell remains, and is found pushed to one side of the fat globule, between it and the cell envelope, surrounded it may be by a little of the cell protoplasm. The rest of the protoplasm appears to have been used up in the formation of the fat globule (Figs. 46, 48). The formation of fat in these cells thus resembles to some extent the production of mucin in a cell of a mucous gland, but in the latter case the protoplasm of the cell is not used up to the same extent as in the fat cell, but remains in the form of bars between the still separate granules of mucinous substance.

We have already seen (page 18) that this fat is composed chiefly of olein, stearin and palmitin (combinations of fatty acids with glycerin), and that the differences in the fat of different animals is due to the varying proportions in which these three neutral fats are present. They have different melting points, palmitin, for instance, melting at a lower temperature than stearin does, whilst olein is fluid at all ordinary temperatures. Thus the fat of the sheep, which contains a large proportion of stearin, has a relatively high melting point of 50°, which accounts for the rapidity with which mutton fat congeals; while the fat of dogs, which has a large proportion of olein in its composition, has a melting point of 22°. Human fat has a melting point varying from 15° to 22° for that found beneath the skin to 25° for the perirenal fat; while the fat of the ox melts at about 40°. The fat of the food, we have seen, undergoes emulsification in the intestine, and is also in part split up by the fat-splitting ferment of the pancreatic secretion—steapsin—into glycerin and fatty acids. A large proportion of the food fats is absorbed, not in the form of fat itself, but as fatty acid, which, however, becomes reconverted to fat by synthesis with glycerin in the columnar epithelium of the villi. Such a synthesis, however, has been shown to be independent of the presence of glycerin derived from the food, for if fatty acids be substituted for the fat of the food in the case of a dog (Munk) as much fat enters the lacteals as if fat itself had been given, the columnar epithelial cells containing the usual globules of fat, which must have resulted from synthesis of the fatty acids with glycerin provided in some way by the cells themselves. This is the more interesting as glycerin is not found free in the animal body.

From the lacteals, the fat absorbed from the alimentary canal passes into the thoracic duct and thence into the blood-stream,

from which it rapidly disappears after a meal. It is to be noted, however, that this constituent of the food reaches the general blood-stream directly, that is to say, it does not first pass through the liver, as we saw the proteids and carbohydrates did. We may then ask ourselves—What becomes of the fat which thus enters the blood-stream and so rapidly disappears from it? and we shall find that though some of it *may* be directly stored up as fat in the tissues, the greater part, and it may be the whole, is oxidised mainly in the muscles to carbonic acid and water, the energy set free taking the form of heat or work. If we ask ourselves again—From what classes of food-stuffs is the fat of the body formed? we must answer that it may be formed from any of them—proteids, carbohydrates and fats. We may now proceed to go into the matter a little more fully and consider some of the evidence in support of the above statements.

Formation of fat from the fat of the food.—It would seem at first sight reasonable to suppose that the fat of the food carried to the tissues in the blood-stream was seized upon by the cells of adipose tissue and stored within them without further change, to be given out again as the needs of the organism required it, but there are certain considerations which will make us pause in coming to such a conclusion. It is found that an animal stores up in its tissues the same kind of fat, *i.e.*, the fat peculiar to its species, whatever kind of fat it may be fed on. Thus if a man live upon mutton, the fat he stores up will not have the composition of mutton fat but of human fat—the fact that there was a large proportion of stearin in the fat he ate will not lead to a correspondingly large proportion of stearin in the fat he stores up, which will be found to have the usual amount of olein in it and a low, not a high melting point. In this case, if the fat of the food has been stored up as the fat of the body, it must first have undergone some change, *e.g.*, the superfluous stearin must have been broken down and its products of decomposition built up again to yield the constituents of the fat normal in the human body. Furthermore, if a dog, whose natural fat is a mixture of palmitin, stearin and olein, be starved and then fed with lean meat and a fat containing olein and palmitin alone, the body fat laid down does not differ from the normal, but consists of the usual three fats. In this case we may, if we like, suppose the stearin to be built up from the decomposition products of some of the olein and palmitin, but as it is conclusively proved that fat may be formed from proteid, it is much easier to conclude that it has this origin, and if so the palmitin and olein of the mixed fat may have been

produced in the same way also. As fat can be formed from proteids, the administration of fat may lead to the laying down of body fat, not by being itself directly stored, but by its oxidation sparing the proteids, which are thus rendered available as fat producers, and this seems to be rendered the more likely by the observations we have recorded above as to the little influence on the composition of the body fat exercised by the nature of the fat given as food.

Fats can also be formed from carbohydrates, as we have seen, and it is clear from the ordinary experiences of fattening animals that only a small amount of the fat laid on can be derived directly from the fat of the food. The fat in the milk of a cow also is much greater than can be accounted for by the fat present in the food, and a suckling dog fed on lean meat produces more fat in its milk than can be accounted for by the carbohydrates and fats of its food. Are we justified then in saying that any of the body fat is directly derived from the fat of the food? The answer to this must certainly be that it may be, for if a starved dog be fed with plenty of fat and little proteid it lays on more fat than can be accounted for by the proteid corresponding to the amount of nitrogen excreted, even supposing that the whole of the carbon of the disintegrated proteid had been stored up as fat. With a diet of pure fat, again, more carbon is retained than could have been derived from the proteids of the tissues as measured by the nitrogenous excretion. Furthermore, if a starved dog be fed with excess of mutton fat and sufficient proteid, the body fat laid down bears a striking similarity to mutton fat in its melting point and composition as contrasted with the ordinary body fat of the species; and in the same way the administration with the food of other forms of fat foreign to the animal fed, such as spermaceti, rape oil, and linseed oil, will lead to their being to some extent laid down along with the body fat. These are instances, however, of somewhat abnormal nutrition and cannot be taken as an absolute indication of what takes place under normal conditions.

Formation of fat from proteids.—Inasmuch as proteid is poorer in nitrogen and richer in carbon than the urea which is derived from it, it follows that only a portion of the carbon the proteid contains is excreted in the form of urea. That the remainder can be stored up as fat has been demonstrated by the following experiment of Pettenkofer and Voit. A dog was fed entirely on lean meat (which contains too small an amount of fat or carbohydrate to interfere with the proof) and it was found on comparing the results of analyses of the food and excreta that a

considerable proportion of the carbon ingested was retained in the body, presumably in the form of fat (which contains nearly all the non-proteid carbon of the body). The following table represents the results of the analysis in the experiment on a dog fed on lean meat. The equation gives the result of the first day's feeding:—

	Grms. N.	Grms. C.
Taken in the food..............	68·0	250·4
Given out in urine, fæces, and respiration..................	67·9	207·4
Difference.........	+0·1	+43·0

Of course the surplus carbon derived from the proteid molecule is not necessarily retained in this way. The economy of the animal body may necessitate its immediate conversion to CO_2 in the production of heat or work, in which case the deficit in the carbon excreted would not take place, and none of the carbon would be laid down as fat; but it is sufficient for the proof of the point in question, *i.e.*, that fat is produced from proteid, that in certain cases the surplus carbon is shown to be retained in this form.

There are other reasons, also, for believing that fat is produced from proteid. We have already mentioned that the fat of the milk of suckling animals is increased by a proteid diet. In the ripening of cheese the fat is produced at the expense of the proteid. Similarly, the fatty acids of adipocere are produced at the expense of the proteids of the flesh. In phosphorus poisoning fat is found in the liver and tissues of an animal though it be starving. One of the most convincing proofs of the origin of fat from proteid is derived from the experiment in which the eggs of the fly-maggot are allowed to develop on blood-clot. The maggots when fully grown contain ten times as much fat as was originally present in the eggs and the clot together.

At one time many physiologists were sufficiently impressed with the production of fat from proteid to hold the view that it was the exclusive source of fat production, and that the carbohydrates of the food, even if they led to the laying down of fat in the body, only did so by protecting the carbonaceous residue of the proteid molecule from oxidation, and so allowing it to be stored up as fat. This, however, has been shown to be an extreme view and is not now entertained. As we have already seen from the experiment of Gilbert and Lawes on pigs, fat is undoubtedly produced from the carbohydrates of the food.

Formation of fat from carbohydrates.—The formation of fat from carbohydrates has already been referred to under the heading of "Carbohydrate Metabolism" (page 473), and we need only say here, that though it is certain that the fattening properties of carbohydrates depend largely on their protecting the proteids and fats of the food from oxidation by being oxidised in their place, and so allowing fat to be laid down from them, it is equally certain, as the experiment just quoted shows, that an amount of fat may be laid down on a carbohydrate and proteid diet much in excess of what could possibly have been derived from the carbon residue of the proteid. The fat must therefore have been derived from the carbohydrates of the food, probably by their being broken down to simpler compounds, which are reconstructed to form fat, oxygen being lost in the process. Apart from direct experimental evidence, however, it is almost too obvious a fact that carbohydrates can be converted into fat to need demonstration. Such herbivora as sheep and oxen get fat upon a purely grass diet, in which the amount of fat and proteid is clearly insufficient to account for the fat stored up, and in which the carbohydrate element is predominant.

The **secretion of milk.**—Milk may be regarded as the only perfect food, *i.e.*, it contains the various alimentary principles—proteids, carbohydrates, fats, salts and water—in the proportions requisite for complete nutrition. As the metabolic processes in the mammary gland leading to its production are so closely related to those which we have been considering, we may appropriately close this section of our study of metabolism with a short account of the histology of the gland and the changes which take place in the cells during lactation.

The mammary gland is of the compound racemose type, and like the sweat glands is developed as an ingrowth or downgrowth of the Malpighian layer of the epidermis. In the human subject it consists of some twenty subdivisions separated by fibrous septa and opening on to the surface of the nipple by independent ducts. Each of the lobes is divided by connective tissue septa into secondary lobes, and these again into lobules, the original ducts subdividing again and again in the usual way in the course of their distribution to the ultimate alveoli of the lobules. The alveoli themselves on section are somewhat irregularly round in shape and are lined with an epithelium which varies in character with the functional condition of the gland. During the period of lactation when milk is being secreted the cells are tall and somewhat columnar in shape, their conical, narrower, internal

ends projecting in varying degrees into a considerable lumen, which is thus more or less irregular in contour. Within the lumen are to be seen the fat globules of the milk, of various sizes, and sometimes small fragments of epithelial cells. The lining cells exhibit a well marked nucleus near their base, which rests upon a basement membrane, while in the conical projecting portion of one of them may be seen one or more fat globules apparently on the point of being extruded into the lumen. An additional nucleus may sometimes also be seen in the inner part of the cell, and this inner part frequently becomes detached as a whole; the protoplasmic fragment set free, containing a nucleus and one or more fat globules, floating off in the rest of the secretion. In this way a still more irregular contour may be given to the lumen, as shown in Fig. 300, and this stage in the secretion may be taken as typical of the state of the gland during lactation. All the alveoli, however, are not seen to be in this condition, even in the lactating gland, the cells of some of them being in the condition characteristic of the quiescence between two suckling periods. It is to be noted, however, that though in different lobules the cells may vary in height, the cells of alveoli in the same lobule are of the same height.

Fig. 300.—Section of Mammary Gland during Lactation.

In a resting mammary gland, *i.e.*, between the periods of lactation, the alveoli are found to differ considerably from the above. The lumen is larger, empty and surrounded by cells which are cubical or even flattened, granular and nucleated, reminding one somewhat of those lining the alveoli of the undistended fœtal lung.

A condition differing from either the active or quiescent state is found before pregnancy has yet occurred. In this case the alveoli consist of solid columns of small polyhedral nucleated cells, among which there is of course no lumen, and the alveoli themselves are smaller and less numerous than in the suckling gland. When pregnancy occurs the gland as a whole exhibits rapid growth, new alveoli being formed by budding, but for a time

remaining solid. Previous to parturition the central cells undergo changes of a fatty nature and before or after birth are thrown off, leaving a single layer of cells lining the alveolus, which naturally now possesses a lumen. These cells thus discarded constitute the *colostrum corpuscles* of the first milk; somewhat similar cells filled with fat globules occurring later in the milk are perhaps of the nature of leucocytes which have reached the lumen of the alveolus from the surrounding connective tissue, and thus may be regarded as analogous to the salivary corpuscles.

The main ducts of the mammary gland are lined by cubical or columnar cells, which become flattened in the ductules opening into the alveoli. Prior to opening on to the surface of the nipple the main ducts each exhibit a flask-like enlargement or sinus. The ductules also frequently exhibit enlargements upon them within the lobules.

Characters and composition of milk.—Human milk has a specific gravity of 1028 to 1034 and is slightly alkaline in reaction when perfectly fresh. As already stated, it contains the various food constituents in the proportions required for perfect nutrition. These proportions, however, will naturally vary in the milk of different animals.

1. *Proteids.*—These include *caseinogen,** with *lactglobulin* and *lactalbumin* in small quantities, the latter of which differs slightly from serum-albumin in its solubilities, rotatory power, and the temperature at which it coagulates. Some of the characters of *caseinogen,* the chief proteid, have been already mentioned (page 4). The clotting of milk results from the action of the rennin ferment, whereby the caseinogen becomes converted to insoluble casein. It is not, however, a simple conversion of one proteid to another of a more insoluble nature, as the process is analogous to the conversion of fibrinogen to fibrin (page 247). That is to say, the caseinogen is split by the rennin into two parts, one of which goes to form the *curd* and is called casein, while the other passes into the *whey* and has been termed "whey proteid" by Hammarsten. This proteid is not coagulated by heat and has several resemblances to peptone and proteose, but it does not give the rose-pink biuret reaction. "Whey proteid" corresponds to the "lacto-protein" of some authors. The curd or clot consists of the casein and the entangled fat globules; the whey contains the other proteids, sugar and salts.

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* It is well to apply the term *Caseinogen* to the proteid in milk which is acted upon by the rennin ferment, and the term *Casein* to the product of the action in the clot, but it should be remembered that this nomenclature is not universally accepted: it has, however, the advantage of being in line with the terms fibrinogen and fibrin, myosinogen and myosin.

The presence of a salt of calcium is necessary for the formation of a clot, calcium phosphate being the one mostly present in milk, and it appears that there are two stages in the clotting. In the first of these the caseinogen is converted by the rennin ferment into "soluble casein," and in the second this soluble casein combines with the calcium salt and is precipitated as a caseate of lime, for if a portion of a solution of pure caseinogen be placed in a test-tube, rennet added, and the mixture kept at 40° C. no clotting occurs, and yet the caseinogen has undergone a change, for if the mixture be now boiled so as to destroy the ferment, cooled, and a little calcium chloride added, clotting takes place (Ringer). The addition of lime salts to a solution of caseinogen which has not been exposed to the action of the rennin ferment has no effect.

This clotting of milk by rennin must be distinguished from the precipitation of caseinogen which occurs when milk sours from the production of lactic acid, or has acid added to it, or is treated with excess of neutral salts. If milk be exposed to the air it undergoes the lactic acid fermentation and caseinogen is precipitated, the fat of the milk being entangled in the precipitate as before. This precipitation of caseinogen by acid is not prevented by the addition of a soluble oxalate (which decalcifies the fluid) as the "clotting" of milk is, and the curd obtained by precipitation with acid cannot be utilised in the manufacture of cheese. Moreover, if caseinogen prepared by precipitation and free from lime salts be redissolved and treated with rennet it will not clot, but clotting takes place readily if calcium phosphate be added. In other words, when caseinogen is precipitated by acid it is precipitated as caseinogen; when it forms a clot under the influence of rennin it has undergone a radical change and part of it at least has united with calcium.

Caseinogen bears many of the characters of a nucleo-proteid. When broken down it does not yield bodies of the purin ($C_5H_4N_4$) or xanthin series, like the typical members of that type. It is commonly held to be a proteid in combination with a pseudo-nuclein. It is not coagulated by heat.

2. *Fats.*—As in adipose tissue, the chief fats in milk are olein, palmitin and stearin, but small quantities of other fats are also present. The proportion of the fats to each other varies in different animals. Traces of lecithin and cholesterin are also found. The fat is present in the form of an emulsion, the suspended globules varying greatly in size. On standing, they rise to the surface of the milk and collect there in the form of cream, but they still remain separated from each other.

3. *Sugar.*—Lactose, or sugar of milk, occurs in relatively considerable quantity in human milk. It differs from dextrose in being less soluble in water and insoluble in alcohol, neither will it undergo direct alcoholic fermentation under the influence of yeast. It readily, however, undergoes fermentation to lactic acid, as in the souring of milk, the caseinogen being precipitated when sufficient acid has been produced. Though lactose itself does not ferment with yeast, milk can undergo an alcoholic fermentation under the influence of certain ferments, as in the preparation of koumiss and kephir in Russia from mare's milk. When hydrolysed, lactose splits into one molecule of dextrose and one of galactose.

4. *Salts.*—Of the presence of calcium phosphate in connection with the curdling of milk we have already spoken. Potassium and sodium chlorides, with a small amount of magnesium phosphate, are also present. Iron is also found, and traces of sulpho-cyanide.

The following table shows the average composition of the milk in different animals, but it must be remembered that the composition of the milk in the same animal varies considerably from time to time:—

Average Composition of Milk in different Animals.

	Woman.	Cow.	Mare.	Bitch.
Casein, &c.	2	4	2·5	10
Fats	2·75	4	2	10
Sugar	5	4·4	5	3·5
Salts	·25	·6	·5	·5
Total Solids	10	13	10	24
Water	90	87	90	76

It will be observed that human milk differs from that of the cow in the lower percentage of proteids and higher percentage of sugar. A woman may produce about three-fourths of a litre of milk during twenty hours and a cow about ten litres per diem.

Colostrum.—The milk secreted just before and after parturition differs considerably from ordinary milk. It is yellower and more alkaline, and contains little or no caseinogen but a large quantity of lactalbumin and globulin, and hence will coagulate on heating. Under the microscope it is distinguished by the presence of the so-called *colostrum corpuscles.* These are large, coarsely-granular, nucleated, refractile cells, many of which are seen to be loaded

with fat globules. Some of them appear to resemble leucocytes, and under suitable conditions of temperature may exhibit amœboid movements; others appear to be cells simply undergoing disintegration; while others appear to be merely fragments of cells. According to some authors the colostrum corpuscles represent the degenerating central cells of the original solid tubules of the gland, and no doubt many of them have this origin. Those which exhibit amœboid movements, however, one might more reasonably regard as leucocytes which have penetrated the alveoli from the surrounding connective tissue. Some of these colostrum corpuscles, again, may be the discarded central ends of the alveolar cells which at an early stage of the process of lactation contain fat droplets and project into the alveolar lumen.

Secretion by the gland cells.—In what way does the material accumulated in the gland cells leave them to take its place in the milk? This is a question which has received more than one answer, largely on account of the presence of colostrum corpuscles in milk and the appearances seen in the alveoli in the earlier stages of lactation which have been already described. By some it has been contended that the cells, loaded with the materials of secretion, are set free much as the cells are in a sebaceous gland, and undergo disintegration within the alveoli, the constituents they contain being thereby liberated. This view evidently has its origin in a consideration of what takes place in the sebaceous glands and in the mammary gland itself, whereby the solid tubules become converted to alveoli through the central cells becoming detached and degenerated; but such a method of production would entail, according to Heidenhain, a renewal by multiplication of the cells of the alveoli five times in every twenty-four hours to account for the solids of milk, and of such a multiplication there is no evidence. Others again, observing the elongation of the alveolar cells and the accumulation of secretory products in their projecting ends in an early stage of the development of the secretion, have considered that the free end becomes detached (perhaps by some imperfect method of division) and thrown off to join the general contents of the alveolus, in which it undergoes disintegration, the accumulated products being set free. These contributions of the cells or part of them to the milk are of course assumed to be accompanied with the flow of fluid containing salts, &c., through the lining cells of the alveoli to make up the whole milk. A third view is that the cells may excrete the materials into the lumen in the same way as other gland cells do without undergoing any distinct histological disruption. The first of these three views we may perhaps put on one side at once as having

scarcely a *prima facie* case. With regard to the other two, there seems to be some reason for taking up a position between them, for undoubtedly such a breaking off of the loaded ends of the cells does occur, and the irregular lumen which is often to be seen is the result of this breaking off; but it does not follow that this breaking away of a portion of the cell is repeated in the same cell. It may be that it is comparable to the "dehiscence" of the "cap" of an ordinary goblet cell on an epithelial surface after it has become loaded with mucinous granules, and that after it is once separated the subsequently secreted material is extruded from it as from a goblet cell without much further disruption. We might suppose then that a cell of the mammary alveolus in an early stage of its active life underwent some such initial disruption which was not repeated in itself, but that the same disruption occurred again in the younger cell which replaced it when its life was ended. If we accept this view, we should say that the breaking off of a portion of the cells loaded with secretion occurred incidentally and had its influence on the composition of milk (*e.g.*, accounting perhaps for the presence of nuclein in it among other things), but that for the most part the secretory material was passed into the alveolar lumen, as in other glands, without further disruption of the cell. Of the secretory material thus elaborated in the cell, the fat appears in the most obvious form, but no doubt the proteid and carbohydrate elements are deposited in the cell substance in a similar manner.

Formation of the organic constituents of the milk.—"The blood is the ultimate source of milk, but it becomes milk only through the activity of the cell, and this activity consists largely in a metabolic manufacture by the cell, and in the cell, of the common things brought by the blood into the special things present in the milk" (Foster). Thus we may suppose the caseinogen to be formed in the mammary cells by a molecular change in the serum-albumin or globulin of the blood, as caseinogen does not exist as such in the blood, or indeed in any part of the body except the mammary gland. Similarly, the fat of the milk appears to be formed in the gland cells and not to be simply withdrawn as fat from the blood-stream and lodged in the cell protoplasm. There is reason to regard it as formed from proteids by the metabolic activity of the gland cells, for a bitch fed on meat alone produces more fat in her milk than she could possibly have taken with her food. Moreover, while the quantity of fat in the milk is directly increased by the administration of proteids, it is, on the contrary, diminished on a fatty diet; but though in man and carnivora the proteids of the food are the main source of the fat of the milk,

in the lactating herbivora the carbohydrates will be largely drawn upon. The lactose, or sugar of milk, like the caseinogen, is found nowhere else in the body, and this again may be taken as an indication that it is formed in the gland cells themselves. Moreover, it continues to be secreted in normal amount in the milk of carnivora which are fed entirely upon proteid, so that its production is independent of the presence of carbohydrate in the food.

We thus see that in the mammary gland we have taking place side by side in the same cell the construction of proteid, carbohydrate and fat—the three chief organic constituents of the food—and "we may look upon what is taking place in the mammary cell as a picture of what is going on in various living tissues. If the fat of the milk were not ejected from the mammary cell, the mammary gland would become a mass of adipose tissue, especially if by a slight change in the metabolism the production of fat were exalted at the expense of the production of casein or milk-sugar. If, again, by a similar slight change, the milk-sugar were accumulated rather than the fat or proteid, we should have a result which, by an easy step, would bring us to glycogenic tissue. Lastly, if the proteid accumulation were greater than the fatty or the saccharine, these being carried off in some way or other, we should have an image of the nutrition of such a tissue as muscle, in which the proteid constituent is in excess of the others" (Foster).

Effect of various conditions on the secretion of milk.—That the secretion of milk is affected by the *state of the nervous system* in lactating women is well known, but the nervous mechanism involved has not yet been satisfactorily worked out. When the nerves in animals have been cut the secretion still continues, according to some observers in increased quantity, while others have found it diminished. Stimulation of the cut nerves appears to diminish the amount of the secretion, but there is nothing to indicate that this is not the result of the vaso-motor changes induced. The influence of *diet* upon the secretion of milk, both as regards quantity and quality, is well marked. Generally speaking, a liberal diet increases the amount and richness of the milk secreted, and in man and carnivora it is the increase in the proteid element in the food that is so efficacious in producing this result. Moreover, it is the fat in the milk that is especially affected by the increase of the proteid in the food rather than the caseinogen and lactalbumin, though these are both increased by a diet rich in proteid, as well as the sugar of the milk. Among *drugs*, while atropin in small doses reduces the quantity of milk secreted, the secretion is more concentrated: in larger doses it

arrests it altogether. Pilocarpin, while increasing most of the secretions of the body, is said to have little or no effect on the secretion of milk.

The Income and Expenditure of the Body.

In the sections above we have made some attempt to study the metabolic changes in the body qualitatively, but we may approach the matter from another point of view, and by comparing the income and expenditure of the body for a given period draw conclusions of some value as to what has taken place. We may term this the quantitative or statistical method of studying metabolism.

The income of the body will consist of the food and oxygen, but it must be borne in mind that the apparent food income is not the real one; the fæces, consisting of undigested matter for the most part, require to be deducted from it. In such an income we shall find the elements nitrogen, carbon, hydrogen, oxygen, sulphur, phosphorus, salts and water contained in the food, in addition to the oxygen taken in by the lungs. The output will consist of the various excreta and the water and carbon dioxide lost by the lungs. It is usually sufficient for practical purposes if the nitrogen and carbon of the income and output of the body are compared.

By *complete nutritive equilibrium* is meant the condition of affairs which obtains when the income and expenditure exactly balance each other, the body neither losing nor gaining weight, and such a condition of complete equilibrium is expressed in the following table, in which the C and N income and expenditure of a man weighing 70 kilos are compared.

Incomings.			Outgoings.		
Food.	N.	C.	Excreta.	N.	C.
Proteids .... 100 grms.	15·5	53	Urine	14·4	6·16
Fats .... 100 "	...	79	Fæces	1·1	10·84
Carbohydrates... 250 "	...	93	Respiration...	...	208·00
	15·5	225		15·5	225

Such a table as the above forms a sort of balance-sheet—a debtor and creditor account—from which, as we shall see immediately, we can often draw important inferences. Instead

of this complete equilibrium there may be a gain in weight during the period of the experiment, and it may be found, on comparing the ingesta and egesta, that whereas the nitrogen of the food exactly corresponds in amount with the nitrogen excreted, the carbon shows a deficit, *i.e.*, there is a less quantity of this excreted than was taken in. Such a body is said to be in *nitrogenous equilibrium* because the nitrogen excreted corresponds in amount with the nitrogen taken in; but clearly it is not in a state of carbon equilibrium, for there is a carbon deficit in the egesta—in the case recorded in the accompanying table of 39·8 grms.

Incomings.			Outgoings.		
Food.	N.	C.	Excreta.	N.	C.
Proteids .... 137 grms.	19·5	315·5	Urine	17·4	12·6
Fats .... 117 "	...		Fæces	2·1	14·5
Carbohydrates... 352 "	..		Respiration...	...	248·6
	19·5	315·5		19·5	275·7

From such a table as this we may infer that the nitrogen-holding living substance of the body (*e.g.*, muscle) is being neither increased nor diminished in amount, but inasmuch as less carbon is leaving the body than entering it, some is being retained and laid on, probably in the form of fat, and, conversely, if more carbon had been leaving the body than entered it in the food we should have inferred that the fat of the body was diminishing in amount.

To further illustrate the use of such balance-sheets we may suppose a third case, in which the animal has gained in weight during the period of the experiment, but in which there is neither nitrogenous nor carbon equilibrium, the amount of both N and C in the egesta being less than that of the same substances in the ingesta. We infer, to start with, in such a case that the deficit in the egesta of N has been stored up in the form of muscle (chiefly), and the amount of muscle or flesh so laid on is easily calculated, as we shall see immediately. We may next consider the carbon deficit in the egesta, and here the first source of possible error occurs. We must not in the same way regard this as proportionate to the fat laid on, as we did when there was nitrogenous equilibrium, for some of the carbon has been required to make up the proteid of the flesh laid on, which contains C as well as N. We must

therefore deduct the amount of C required for the stored-up proteid from the C deficit in the egesta, and the remainder will give the amount of C which we may regard as having been retained as fat (we estimate it as fat for the glycogen of the body is inconsiderable, and in the same way, though the nitrogen might be stored to some extent in the liver or elsewhere, the muscles are the seat of the main loss or gain of proteid material).

In estimating the N and C value of foodstuffs and translating the N and C of the excreta into terms of proteid, fat, &c., the following data are required. Proteids contain 15 to 17 per cent. of N and 50 to 55 per cent. of C, fat contains 76·5 per cent. C, and carbohydrates (starch and sugar) 40 to 45 per cent. C. As the amount of proteids, fats and carbohydrates in the various foodstuffs has already been worked out, it is thus easy to calculate the amount of N and C in the ingesta. In translating the N of the egesta, either in the way of excess or deficit, into terms of flesh lost or laid on, as proteid contains 16 per cent. of N we multiply the N excess or deficit by 6·25 to find the amount of proteid lost or gained, and as, roughly speaking, one-fifth of muscle is proteid we may translate this again into flesh lost or laid on by multiplying by five, or we may make a more direct calculation and regard a grm. of N in the urine as corresponding to 30 grms. of flesh, as flesh contains about 3·4 grms. N.

In translating the C excess or deficit into terms of fat lost or laid on we must first (unless there is nitrogenous equilibrium) deduct the C which the proteid metabolised would contain, which we may put at about 53 per cent. of such proteid. The remainder multiplied by 1·3 will give the fat lost or laid on, as fat contains 76·5 per cent. C.

The following table shows the percentage amount of proteid, fat and carbohydrate in some of the commoner foodstuffs:—

Foodstuffs.	Proteid.	Fat.	Carbohydrate.
Potatoes	2	0·1	20
Cows' Milk	4	4·0	4·4
Rice	8	0·9	77
Wheat	12	1·7	70
White of Eggs	13	0·3	...
Yolk of Eggs	16	32·0	...
Fat Beef	17	26·0	...
Fish (Pike)	18	·5	...
Lean Beef	21	1·5	...
Peas	23	1·8	58

Proportions of constituents of ordinary diet.—We have already seen that an ordinary mixed diet for man consists of proteids, carbohydrates and fats, together with a certain amount of salts and water. In such a mixed diet the organic constituents are usually present in the proportion of about one part of proteid to four to six parts of non-proteid: and of these latter, about one part of fat goes with five to ten of carbohydrate. The following might represent the proportions in the daily diet of an adult doing hard muscular work:—

118	grms.	proteid.
56	"	fat.
500	"	carbohydrate (Voit).

But, as we shall see, the amount of the food constituents required varies with different conditions—*e.g.*, of work and rest, &c.,—and to this we shall return when "dietetics" are under consideration. Though the proportions of the organic constituents to each other which we have given may be regarded as the most general, they are by no means constantly adhered to. Thus many races of men, such as the Asiatics, consume a far greater proportion of non-proteid material than that given, while in parts of the world where meat is plentiful the proportion of proteid in the diet is correspondingly large. Again, the wealth or poverty of members of the same community makes a difference, the rich consuming more proteid and fat, the poor drawing largely upon the carbohydrates. Vegetarians also depart considerably from the usual proportion, as in order to obtain the required amount of proteid in their diet they have to consume at the same time a very large proportion of carbohydrate. In the same way, on a diet principally of meat the amount of proteid and fat is high compared with that of the carbohydrate.

Heat value of foods.—The calorific value of a mixed diet is obtained by multiplying the number of grms. of its organic constituents by a number representing the amount of heat produced by the oxidation of one grm. of the substance to CO_2 and water or to urea. Now, the amount of heat produced by the oxidation of one grm. of proteid to urea is 4124 grm. degrees, or 4124 *calories* as it is termed, the amount of heat produced by the oxidation of one grm. of fat is 9321 calories, and of one grm. of carbohydrates (starch) 4116 calories. In kilogram degrees these will be 4·124, 9·321 and 4·116 *kilo-calories* respectively. With these figures, which have been exactly determined, by us, we may estimate the calorific value of such a diet as that given above, thus:—

105*	grms.	proteid	×	4·1	= 430
56	"	fat	×	9·3	= 520
500	"	carbohydrate ...	×	4·1	= 2050
					3000 kilo-calories.

Thus 3000 kilo-calories or 3,000,000 calories may be taken to represent the energy value of the daily food of an average man of 70 kilos, doing hard work.

As 1 grm. of fat in its combustion produces 9·3 kilo-calories, as compared with 4·1 produced by the combustion of an equal amount either of proteid or starch, it follows that the combustion of 100 grms. of fat will produce as much energy as the combustion of 227 grms. of either proteid or starch, and 100 grms. of fat are thus said to have the same "isodynamic value" as 227 grms of either of these substances.

Metabolism during inanition.—The simplest condition of metabolism we can study is found in a starving animal, one from which food is altogether withheld, for here we have only to deal with the metabolic changes taking place in the tissues themselves, and not with the metabolism of foodstuffs either before or after they reach the tissues. When food is altogether withheld from an animal, though the excretions are necessarily diminished in amount, they still continue, not only from the skin, lungs and kidney, but even to some extent from the bowel; in the latter case consisting of mucus, epithelial cells, altered secretions, &c. The excretions quickly reach a tolerably even level, and after the first day or two a fairly regular loss of weight occurs from day to day. We say after the first day or two, for at first, owing to the food already in the system before the commencement of the period of inanition, the decrease in the amount of the excreta is less marked than it is afterwards. This period at the commencement of starvation, while the proteid previously ingested is being metabolised and the nitrogenous excretion is maintained at a higher level than subsequently, will naturally vary in length according to the previous condition of nutrition. In the case of Voit's dog, this animal was subjected to a series of experiments, in the first of which it was fed, previous to the period of inanition, with 2500 grms. of flesh per diem, in the second with 1500 grms., and in

* It has been shown that some of the products of the combustion of proteid escape in the fæces as well as the urine, so that about 13 grms. of the 118 previously given are not absorbed or assimilated, leaving 105 available for the calculation. Some allowance should also be made, perhaps, for the carbohydrates and fat, which in a mixed diet are not themselves wholly assimilated.

the third with a mixed supply of food containing comparatively little proteid. The result of inanition on the excretion of urea per diem is shown in the following table, and it will be seen that whereas in the first of the series of experiments the excretion of urea did not reach a fairly constant level till the fifth day, this was attained sooner in the second series, and began at once in the third.

Day of Inanition.	Grammes of Urea excreted per Diem.		
	Series 1.	Series 2.	Series 3.
	—	—	—
1	60·1	26·5	13·8
2	24·9	18·6	11·5
3	19·1	15·7	10·2
4	17·3	14·9	12·2
5	12·3	14·8	12·1
6	13·3	12·8	12·6
7	12·5	12·9	11·3
8	10·1	12·1	10·7

This excretion of urea remains fairly constant, though of gradually decreasing amount daily as starvation proceeds, but a sudden rise in the excretion frequently takes place in the later stages of the experiment. This is attributable to the fact that the fat of the body has now become completely used up and the whole energy and heat of the body has to be derived from the proteid tissues themselves. From a somewhat similar cause there may be in herbivora at the commencement of a period of inanition an increase in the amount of urea excreted instead of a diminution. The explanation of this is to be found in the fact that these animals, when their ordinary food is withheld, practically become carnivora, as they are reduced to living on their own tissues. Later on, when the fat of the body is exhausted and the whole of the energy and heat has to be derived from proteid tissue, an increase in the nitrogenous excretion may be again observed, as in carnivora.

Temperature in starvation.—The normal temperature of the body of a starving animal is maintained for some time through the oxidation of the fat and proteids of its body, but in the later stages, when the supply of material for oxidation begins to fail, the temperature sinks and then falls rapidly. In addition to the failure of the supply of nutriment from the tissues, and as a result

of it, the heat regulating functions of the nervous system towards the end become impaired, and this increases the fall in temperature, the animal practically dying to a large extent of cold. Death can be delayed for some time in fact, as we might expect, by keeping the body artificially warmed, so that such substances as are still available for nutrition may be reserved for the production of energy and not wasted in the production of heat; but this of course will only avail for a certain time and death must inevitably close the scene.

Loss in different tissues during starvation.—Broadly speaking, in starvation the less important tissues and organs are drawn upon for the nourishment of those of supreme necessity for the continuance of life, and we thus find that while the fat of the body, the great metabolic glands, such as the spleen and liver, and the muscles are in turn heavily mulcted, the heart and central nervous system suffer little loss, but are maintained at nearly their normal weight till the very end. Nor do they, even when the supply of material from the other tissues has come to an end, contribute their own quota to the impoverished blood; they fall to pieces, as it were, functionally when their supply of nutriment from the blood is at an end, and death quickly results.

The following table shows the percentage of loss in the different organs of a cat, killed after thirteen days starvation (Voit):—

	In 100 parts of Fresh Organs.
Fat	97
Spleen	67
Liver	54
Muscles	31
Blood	27
Intestines	18
Bones	14
Heart	3
Central Nervous System	3

It will be seen from this table that there is a very marked difference between the percentage of loss in the heart and central nervous system (3) and the much higher percentages in the case of the other tissues and organs. The very great loss of adipose tissue (97 per cent.) and the still great, though not so marked, loss in the spleen and liver (67 and 54 per cent.) illustrates the part these play as storehouses of nutritive material, and hence they are amongst the first to be drawn upon. It is perhaps needless to say

that the glycogen stored in the liver and muscles begins to disappear with the commencement of inanition.

Nutrition with a proteid diet.—It might be expected that if a dog which had been previously starved for some time were supplied with an amount of lean meat corresponding to the daily excretion of nitrogen during the period of starvation, the income and loss of nitrogen would then balance each other, and that there would no longer be any waste as far as proteids are concerned. This, however, is not the case. Instead of the loss of nitrogen remaining the same after feeding with a corresponding amount of proteid is commenced, it may rise to nearly double the loss during starvation; more nitrogen, in fact, is given off in the excreta than is supplied to the animal in its food. All the nitrogen supplied in the food is excreted, together with a considerable amount of the tissue nitrogen which was excreted in starvation, so that the animal still loses flesh, nor does it cease to do so until an amount of proteid is given as food equal to some two-and-a-half times the proteid metabolised during starvation, when nitrogenous equilibrium becomes established (Voit).

We thus see that the effect of a purely proteid diet is to greatly stimulate the nitrogenous metabolism of the tissues; whereas carbohydrates and fatty foods have a sparing effect upon proteid metabolism.

The amount of proteid required for the condition of nitrogenous equilibrium is by no means a fixed one but varies with the condition of the body, a well nourished animal requiring much more proteid food to maintain it in a condition of equilibrium than it would if it were in an emaciated state. Thus Voit's dog while in reduced condition could maintain N-equilibrium upon a daily diet of 500 grms. flesh, or about three times the daily loss of nitrogen in starvation. If this amount were increased the animal would lay on flesh until N-equilibrium were again attained, and a further increase would lead to a still further laying on of flesh until the amounts of N ingested and excreted again balanced each other. This process of making increases of constant amount in the proteid supplied is followed by the same result of an increase in flesh laid on, succeeded by N-equilibrium, until gastric disturbances supervene and stop the experiment, it may be at a point when fifteen times as much proteid is being metabolised as during the period of starvation. Voit's dog could maintain nitrogenous equilibrium up to 2500 grms. flesh daily.

Diminution of the amount of proteid supplied leads, in the same way, to the establishment of N-equilibrium on a lower

level, the animal first of all losing flesh until equilibrium is attained, and a further reduction of constant amount leads to a still further loss of flesh until equilibrium is found, the process being capable of repetition until a level is reached when equilibrium can no longer be re-established. As already mentioned, the least quantity of flesh which would maintain Voit's dog in N-equilibrium was about 500 grms. daily.

We see, then, from the foregoing observations that the metabolism of proteid in the body varies very much with the amount supplied as food. In other words, the body tends to live up to the supply of proteid and not to lay any by for future use. Though for a time after an increase has been made in the supply some flesh may be laid on, the organism soon adapts itself to the new conditions and spends as much as it receives, or, as we express it, it attains again a condition of N-equilibrium. In a similar way, when the supply of nitrogenous food is reduced (within certain limits) though flesh is lost for a time the organism soon adapts itself again to the supply, the tissues becoming economical, and equilibrium is again attained.

We may repeat here, what we have already had occasion to inindicate, that there are two chief views as to the way in which the administration of proteid food affects proteid metabolism. According to the first of these a small, fairly constant amount is required to meet the waste of the tissue proteid, this amount becoming built up into the bioplasm to take the place of that which becomes broken down, which, as we may conclude from the table of inanition on page 505, is also fairly constant in amount. The greater part of the circulating proteid, however, is supposed, according to this view, to be metabolised by contact only with the living tissue without at any time forming an integral part of it; this metabolism giving rise to energy in the form of heat only and not of vital manifestations such as movement. It is to the metabolism of this part of the proteid that the old term of "luxus-consumption" was applied, for it was regarded as a wasteful expenditure of material, the exclusive purpose of which it was thought was to supply the proteid tissues and thus produce all the energy set free in the body in the form of movement as opposed to heat, the production of which latter had been considered as due to the metabolism of carbohydrates and fats alone. According to the second view, that of Pflüger, we are to consider that the whole of the proteid becomes built up into tissue proteid previous to its being split up, and thus the distinction between the consumption of tissue and circulating proteid becomes useless. According to this view, an increase in the amount of proteid in the blood leads to an

increased tendency to the breaking down of the actual living substance. It must be borne in mind, however, that when we speak of the breaking down of tissue in this sense we do not mean the bodily destruction of the cells themselves. It is a molecular disintegration and repair in the cells themselves, rather than the removal and renewal at one fell swoop of the individual cells.

We cannot follow the matter further here, but it may be said that there is some experimental evidence to show that only part of the circulating proteid becomes built up into tissue proteid or bioplasm. Moreover, the extent and rapidity of proteid metabolism following excess of proteid in the food is against the idea that all the circulating proteid has had to undergo transformation to tissue proteid before being split up.

The **effects of fatty and carbohydrate foods.**—Having considered nutrition with a purely proteid diet, we should pass to the consideration of nutrition with a purely non-nitrogenous one, were it not that if an animal be fed on this alone it necessarily dies of nitrogen starvation. We are therefore obliged to consider the effects of fats and carbohydrates when they are taken along with proteids.

If fat be added to the proteid supplied to an animal, a smaller amount of the latter is required to secure nitrogenous equilibrium, and if fat be added to an excess of proteid in the diet the attainment of nitrogenous equilibrium will be delayed and more flesh will be put on than otherwise would be the case. We have already had an instance of this power of fat to economise proteid in the record of nitrogen excreted by a starving animal, which we saw showed frequently an increased excretion of N when the fat of the body became exhausted. Proteid, on the other hand, as we have seen, stimulates instead of saving proteid metabolism, and we may now further mention that its effect in increasing metabolism is not limited to proteid metabolism but affects the general metabolism of the body, including that of the fat; so that an excess of proteid alone administered to a fat animal does not lead to a further laying on of fat but to an increased metabolism of that already in its body, and the animal will lose fat while it may be putting on flesh. This is the basis of the Banting cure for corpulence, in which the fats and carbohydrates of the food are largely cut off and the patient is put upon a flesh diet. Carbohydrates, like fats, economise proteids, but to an even greater extent, and they also economise fats. It is needless, perhaps, to say that they are more digestible than fats, but, on the other hand, weight for weight, the fats represent more potential energy.

We have spoken repeatedly of nitrogenous equilibrium, and there is of course a *carbon equilibrium* too. As has been already pointed out, the two do not necessarily go together. An animal may be in nitrogenous equilibrium, but at the same time either losing or gaining carbon—its body fat may be diminishing or it may be laying on fat. The body does not, however, so readily adjust its expenditure to its income in the matter of C as it does in that of N, that is to say carbon equilibrium is less easily attained, nor is it of consequence that it should be otherwise, for the amount of fat in the body is not a matter of vital importance.

If a carnivorous animal be fed on proteid alone it may be kept in a condition of C-equilibrium, but the amount of such proteid required is much in excess of the minimum required for N-equilibrium alone. Voit's dog, which could maintain N-equilibrium upon 500 grms. flesh per diem, required 1500 grms. flesh to maintain carbon equilibrium also—three times as much as it required so far as nitrogen was concerned, and if a man of average weight were fed on lean meat alone he would require some 2000 grms. daily to maintain C-equilibrium—an amount enormously in excess of his nitrogenous necessities. In both these cases a large excess of proteid has to be supplied to provide the carbon* required, and so to prevent the body losing carbon. The same end is much more economically attained by giving a much smaller amount of proteid together with a quantity of carbon containing food sufficient to balance the daily carbon loss.

On a diet of fat, or fat and carbohydrate, though the animal must die from want of N, C-equilibrium is easily maintained for a short time, and fat may even be put on if the food is digested. This, however, is not for long, as a rule, and general starvation and death result.

Gelatin as food.—Gelatin appears to be able to take the place of the circulating proteids which are metabolised by contact with the bioplasm of the tissues, but to be incapable of being built up into the bioplasm itself. This is shown by the fact that when given alone in large quantity, or in combination with non-nitrogenous food, N-equilibrium cannot be attained—there is always an excess of N in the excreta over the amount ingested, and consequently loss of flesh from the body. That it can take the place of the circulating proteid, which is directly metabolised without being previously built up into bioplasm, is shown by the

* It will be remembered that the proteid molecule becomes split up into a nitrogenous and non-nitrogenous moiety, the latter of which may be oxidised at once or stored up as fat or glycogen, while the former represents the urea.

fact that N-equilibrium can be attained with a less amount of ordinary proteid if gelatin be added to the food. Moreover, if an animal be fed on non-proteid food, such as fat, and gelatin be then added to the diet, it is found that less nitrogen waste takes place than before—that allowing for the nitrogen taken in as gelatin, which appears in the excreta in full as urea, less N leaves the body. As it cannot be built up into tissue proteid, the gelatin must have taken the place of some of the circulating proteid and saved it from being metabolised. It has a greater power of sparing proteids in this way than either fats or carbohydrates, and is also a fat sparer, though to a much less extent than either fats or carbohydrates. The explanation of its action seems to be, as indicated above, that it becomes split like the ordinary proteid molecule into a urea and a fat moiety by contact with the bioplasm, thus deriving its power to spare proteids, and when given along with proteids to some extent the body fat; but it is unable to take part in the building up of tissue proteid. Its use in cases of illness is thus understandable—though unable to contribute to the building up of the flesh of the patient, it yet saves the tissues from some of the drain upon them which, in the absence of ordinary proteid food, would otherwise take place.

Effects of salts as food.—"Salts, though affording of themselves little or no energy, are as essential a part of a diet as the energy giving foodstuffs, inasmuch as they in some way or other direct metabolism and the distribution of energy, and this is true not only of the inorganic salines, such as chlorides and phosphates, but also of the so-called extractives. The presence of these bodies, both the simpler inorganic and the more complex organic salts, in the blood or in the extravascular juices or lymph of the tissues is essential to or directs or modifies the metabolic activity of the several tissues. The beneficial effects, as components of special diets, of such things as beef-tea and meat extract, which consist chiefly of salts and extractives, with a very small quantity of albumose or other forms of proteid, and the effects, either beneficial or deleterious, of drugs, both turn in common upon their taking a part of some kind or other in, it may be upon their interference with, metabolic processes. The salts and extractives of a diet may be looked upon as necessary daily medicines, and a medicine as a more or less extraordinary variation in these elements of a diet" (Foster).

Animals rapidly die if they are fed with food from which the salts have been extracted. They exhibit symptoms of weakness and general disturbance of the nervous system, often culminating

in convulsions, and they sometimes die more rapidly from this deprivation of the salts in their food than animals which have been subjected to total starvation. This has been attributed to chronic acid poisoning, from the oxidation of the sulphur of the proteids of the food. Normally, the acid thus produced is neutralised by the phosphates, carbonates and alkali-albuminates of the food, but when these are withdrawn the tissues themselves are drawn upon to provide the necessary basic substances. It is a noticeable fact, too, that part at least of the mineral matters of the food must be present in it in the combination with proteids in which they normally occur. Mice fed on salt-freed casein with lactose and the inorganic salts present in milk will *die*, whereas they can be maintained indefinitely on dessicated milk.

If lime is withheld from the food of young animals rickets results, and pigeons which have been treated in the same way exhibit osteo-porosis (thinness and perforation) of the skull bones and sternum, while the bones concerned with movement suffer very little.

Dietetics.

The normal diet of man consists of a mixture of the three classes of foodstuffs—proteids, carbohydrates and fats—together with salts and water; but it is by no means possible to lay down any hard and fast rule as to the amounts of these substances which should constitute the diet of the average individual, for it by no means follows that men of the same weight, doing the same amount of work, and exposed to the same conditions in other ways, will require the same amount of food, and it is a matter of the commonest experience that they do not. The metabolic activity of two such people may vary very greatly and necessitate a much greater amount of food in the one case than in the other, and this, the personal equation of metabolism, must never be lost sight of. The following tables must therefore be regarded merely as representing supposed average diets and in no way capable of universal application. We can no more conclude in any particular case that a man, because he is of a certain weight, will require a certain amount of proteids, fats and carbohydrates per diem, than we can that he will be able to walk a certain distance or do a certain amount of any other kind of work.

Voit considered that a man of 70 to 75 kilos, working ten hours a day, required per diem—

118*	grms.	proteid	(18·3 grms. N).
56	"	fat	(328 grms. C).
500	"	carbohydrate	

(Potential energy 3035 kilocalories);

while Ranke found that a man of 70 kilos who was not engaged in muscular work required—

100	grms.	proteid	(15·5 grms. N).
100	"	fat	(220 grms. C).
240	"	carbohydrate	

(Potential energy 2310 kilocalories).

The above figures are arrived at by what we may term the method of experiment, in which a series of trials are made upon the body of what may be regarded as an average man, and the diet ascertained upon which he was maintained in health, at the same weight and in nitrogenous equilibrium. We may, however, construct tables by pursuing another method, which may be called the statistical one, in which the nature and amount of the daily food of a very large number of individuals is taken, and the amounts most commonly in use ascertained. In this case we may collect the statistics from those who choose their own diet, or from those who are to some extent upon a special regimen, such as soldiers or prisoners. The former class afford the most profitable data perhaps, though it is to be borne in mind that instinct is not necessarily an infallible guide.

Stewart considers that for a man of 70 kilos "doing fairly hard but not excessive" work, 20 grms. N and 300 grms. C per day constitutes a liberal allowance. He gives the following diet table for a man of 70 kilos—

140	grms.	proteid.
100	"	fat.
350	"	carbohydrate.
30	"	salts.
620		

It is to be remembered, however, that statistics show that nitrogenous equilibrium and good health may be maintained by diets in which the proportion of foodstuffs differ greatly from those given above. The proportions of fat and carbohydrate

* Here no allowance is made for unabsorbed proteid, in order that a comparison may be made with Ranke's diet.

may vary between wide limits, and the proteid can be vastly reduced, provided the non-proteids of the diet are sufficiently increased. And such variations are constantly made in all parts of the world on economic grounds, if for no other reason. But though fiscally economical, such diets are not physiologically so: thus a poor Chinaman living almost entirely on rice will require some 2000 grms. to provide 20 grms. N, and will consume 700 grms. C at the same time, or twice as much as he requires. And a man living chiefly on potatoes is in much the same position, only more so: he requires to eat 5000 grms. to obtain 20 grms. N (about twice the quantity required to afford 300 grms. C). Where meat is plentiful, on the other hand, as in parts of South America and Australia, the amount of proteid in the diet may be considerably larger in proportion to the other constituents than as given in the above tables; but an exclusively proteid diet, or one approximately so, involves an analogous waste to that of the carbohydrate diets just referred to, for to obtain the necessary C some 2000 grms. of lean meat would be required—four times as much, roughly speaking, as would provide 20 N—and an excess of nitrogenous food is thrown on the system, which tends to become loaded with the waste products of the proteid metabolism. A glance at the accompanying table showing the amounts of various foodstuffs required to afford 20 grms. N and 300 grms. C will illustrate these points.

	Grms. required to yield 20 grms. N.	Grms. required to yield 300 grms. C.	Proteid in 100 grms.	Fat in 100 grms.	Carbo-hydrate in 100 grms.	Water in 100 grms.	N in 100 grms.	C in 100 grms.
Cheese (Gruyère)	400	770	31	31	—	34	5	39
Peas (dried)	570	840	22	2	55	15	3·5	35·7
Lean Meat	590	2,230	21	3·5	—	74	3·4	13·5
Wheat Flour	870	750	12	2	70	15	2·3	39·8
Oatmeal	760	740	13	5·5	65	15	2·6	40·3
Eggs	1,040	2,040	11·5	12	—	75	1·9	14·7
Maize	1,080	730	10·5	7	65	15	1·85	40·9
Wheat Bread	1,590	1,340	8	1·5	49	40	1·25	22·4
Rice	2,040	820	5	1	83	10	0·9	36·6
Milk	3,170	4,250	4	4	5	85	0·6	7
Potatoes	5,000	2,860	2	0·15	21	75	0·4	10·5
Good Butter	13,000	430	1	90	—	8	0·15	69

As a general rule, the wealthy incline to liberality as far as proteid and fat are concerned, while the poor depend to a greater extent upon carbohydrates on account of their cheapness.

It is to be noted that the food of carnivora and herbivora, like that of man, contains all three classes of foodstuffs, the difference lying in the proportion in which these are present.

Fats and carbohydrates, allied to each other as they are, are not on that account wholly interchangeable. A diet from which either is excluded is an imperfect one, and thus wheat flour or bread is not as satisfactory a sole food as it appears in the first two columns of the table; for the C is almost entirely derived from carbohydrate, there being only 2% and 1·5% of fat present in the flour and bread respectively. The taking of butter with bread is a practical recognition of this deficiency. The carbohydrates of a mixed diet are represented mainly by the starch of vegetables and cereals, and also to a considerable extent by cane-sugar.

We should err very much, however, if, in selecting the constituents of a diet, we had regard only for the amount of potential energy present in the various substances, as calculated from such a table as the above. This of course constitutes an essential element in the selection of any diet; but it is not the only point to be considered, for apart from the amount of proteid, fat and carbohydrate which any foodstuff may contain, it has a physiological value which may exceed or fall below its apparent value when only its chemical composition is looked at. It is quite clear that however high the value of a foodstuff may appear as far as its potential energy is concerned, *i.e.*, however favourably it stands out in such a table as the above, this value must be greatly discounted if it is not readily digested and applied by the economy with ease for the purposes of nutrition. Thus of any series of different substances it is found that a varying quantity in each case may be recovered from the fæces in an undigested condition, and a correction will be required to be made for such different proportions in estimating the value of the different foods. Furthermore, a proteid in one foodstuff may be converted in the alimentary canal almost entirely to peptone, while in another it tends to be largely split up into leucin, &c., while a carbohydrate may be absorbed as maltose, or give rise to lactic acid. To take a simple instance, cheese and dried peas come out well in the above chemical analysis, but they occupy a very different position from the point of view of physiological utility. The agricultural hind's meal of cheese and bread has a much lower value physiologically than a "cut off the joint" and potatoes, though the potential energy of the meal, as shown by chemical analysis, may be of the same value.

Vegetarian diet.—The substances required for the nutrition of the body—proteids, carbohydrates, fats and salts—can be obtained

from the vegetable as well as from the animal kingdom, but few people advocate limiting the human diet to substances of vegetable origin alone. Most so-called "vegetarians," though drawing largely upon the vegetable kingdom for their food supply, include in their diet such animal products as eggs, milk, butter, cheese, &c., and are thus not entitled, in the strict sense of the word, to be called vegetarians at all. In the present state of our knowledge, or want of knowledge, as to the different effect upon the organism of alimentary principles of animal and vegetable origin, we can only investigate this subject somewhat superficially by comparing the relative amounts of such alimentary principles in a typical vegetable as compared with an ordinary mixed diet, and the relative economy of the two physiologically.

In the case of a man of exclusively vegetarian habits examined by Voit the daily diet was found to contain—

Proteids...........	54	grms. (8·4 N).
Fats...............	22	"
Carbohydrates...	557	"
Cellulose	16	"
Water......	1048	

The fæces on this diet amounted to 333 grms. containing 75 grms. solid matter, as contrasted with 120 to 150 grms. containing 30 to 37 grms. dried solids, as an average with the ordinary mixed feeder. Moreover, there were present in the fæces 7 grms. fat, 19 grms. starch, and 9 grms. cellulose, bringing the amount of each constituent which had been really made use of down to 15 grms. fat, 540 grms. starch, and 7 grms. cellulose. Moreover, the fæces contained 3·46 grms. N, representing 22 grms. undigested proteid, thus reducing the amount of proteid available for purposes of nutrition to 32 grms.

Such a diet as the above, when compared with the mixed diet tables previously given, is clearly deficient in proteids and fat to start with, and still more so when the undigested residue in the fæces is taken into consideration. Though we cannot say that such a reduction in these two constituents is incompatible with health, all the evidence we possess on the subject points to it as a disadvantage. The amount of food undigested, too, besides implying waste, is an indication of the comparative indigestibility of vegetable substances. The proteids of vegetables are generally found in association with relatively large quantities of starch, and these are enclosed in cellulose, which offers considerable resistance

to the action of the digestive juices. It has been estimated, indeed, that while only 3 per cent. of the albumin of food of animal origin remains undigested and is lost in the fæces, as much as 17 per cent. of vegetable albumin is thus lost. This loss of undigested matter by the fæces is characteristic of the strictly vegetarian diet, in which the fæces are always voluminous relatively to the total food ingested. Whatever advantage there may be in this greater intestinal current as a vehicle for carrying away the waste products of metabolism, it does not seem likely that it can compensate for the waste of labour in its management and transport (Foster). It is to be noted, too, that from a purely vegetable diet the animal extractives, which, like salts, have their own proper influence on metabolism, are absent.

We may conclude this short reference to vegetarian diet with the following extracts from Dr Burney Yeo's work :—"If we look to the history of the human race, we see that man has been guided in the selection of his food by the circumstances and conditions with which he has been surrounded. His physical organisation seems peculiarly adapted to enable him to accommodate himself to such food supplies as he may be able to procure, without regard to whether they are derived from the animal or vegetable kingdom.

"In arctic regions, where no vegetable can be procured, man lives entirely on flesh and fat, and in hot countries, where fruits and nutritious vegetables abound and are readily procurable, he consumes these largely. But it is a common error to suppose that the natives of all hot climates live to a great extent, or almost exclusively, on vegetable food; wherever animal food can be readily procured it is, as a rule, taken as food. Of the Pampas Indians, who live in a 'climate which is burning hot in summer,' it is recorded that 'they have neither bread, fruit nor vegetables, but subsist entirely on the flesh of their mares'; and as to the effect of such a diet Sir Francis Stead testifies, 'after I had been riding for three or four months and had lived on beef and water, I found myself in a condition which I can only describe by saying that I felt no exertion could kill me!'

"The Chinese eat fish and pork with their rice, the Japanese eat fowls in great abundance, and the flesh of whales is a very common food in several places among the poorer classes.

"The Arabs who inhabit the Nubian desert subsist entirely on animal food, the Abyssinians eat largely of raw flesh. As to the food of the East African it is stated by Burton that 'the Arabs assert that in these latitudes vegetables cause heartburn and acidity, and that animal food is the most digestible. A man

who can afford it confines himself to flesh, and considers fat the essential element of good living.' Parkes also testifies that the 'natives of some of the hottest countries in the world take immense quantities of both *fats* and starches.'

"Nothing can appear clearer than that man, by his organisation and by the varying circumstances and conditions in which he is placed, is destined to be a *mixed* feeder. He can exist, when absolutely necessary, exclusively on animal food, and he can also exist, when equally necessary and inevitable, exclusively on vegetable food; but in those parts of the world in which he reaches the highest degree of development and civilisation and culture we find him a mixed feeder, taking a portion of his food from the animal and a portion from the vegetable kingdom.

"But although we regard man as essentially an omnivorous animal, we are by no means disposed to deny that at the present time, and in England, the due utilisation of vegetable foods is much neglected, and thus there is far too great a tendency amongst the whole of the population to rely chiefly on animal products for food. It has been estimated that in a suitable mixed dietary not more than one-fourth should consist of animal food; if this proportion be greatly exceeded an undue tax is imposed on the excreting organs to eliminate the products of the transformation of the nitrogenous excess thus introduced into the body; or this eliminating process may be imperfectly accomplished and the result of incomplete or abnormal metamorphosis of superfluous nitrogenous substances may increase a pre-existing tendency, or develop one if it does not already exist, to gouty or other kindred disorders."

Modifications in diet under certain conditions.—1. *Diet for hard labour.*—Inasmuch as an increase in the work done is accompanied by an increase in the heat set free, that is to say, as there is a greater total expenditure of energy, it follows that under conditions of hard labour a greater income of energy in the form of food will be required than during rest. But we are not to consider that the muscles only, or indeed any particular tissue or organ, are to be catered for: the strain falls upon muscles, heart, lungs, nervous system, in fact upon the body generally. Thus a general increase in the normal diet is what is required to meet the circumstances, rather than an increase of any special constituent. The following table from Hultgren and Lantergren shows the average amounts of the different constituents in freely chosen diets of workmen in different countries, and the heat values of the diets—

		Proteid.	Fat.	Carbo-hydrate.	Kilo-calories.
Moderately hard work	Russian Workman (Erisman)	131·8	79·7	583·8	3675·2
	Munich Workman (Forster)	131·9	81·5	457·4	3174·1
	Swedish Workman (H. & L.)	134·4	79·4	522·8	3436
Hard work.....	Swedish Workman (H. & L.)	189	110	714	4726

Voit gives the following diet for a soldier on active service—

Proteid.	Fat.	Carbohydrate.	Kilocalories.
145	100	500	3574·5

2. *Diet in obesity.*—Carbohydrates are the chief fatteners, as the farmer well knows, and in cases of obesity these, and also the fats of the normal diet, must be greatly reduced, but it is not desirable to do away with them altogether. A purely meat diet, though undoubtedly efficacious in attaining the result desired, throws too large an amount of nitrogenous waste upon the organism. The proteids should, however, be relatively increased, as they stimulate the whole metabolism of the body, including that of the fats. The reduction of the carbohydrates and fats of the food, and the increase of the proteids, forms the basis of what is known as the Banting cure for corpulency. Fresh air and exercise, with other hygienic conditions, are of course to be included as part of the treatment. In order to *increase* the fat of the body it is obvious that the treatment must be reversed. A sufficiency of proteid, a plentiful supply of carbohydrates and of fat, especially in the form of butter and milk, together with the avoidance of exercise and such conditions as will lead to an increased metabolism, will conduce to the laying on of fat. But the personal equation of metabolism must not be overlooked, and it is to be noted that of two people under similar conditions of diet, one will frequently remain thin while the other will get fat.

3. *Diet in infancy.*—A growing child requires more food than we should suppose according to its weight, for in order that it may grow its income must exceed its expenditure. Moreover, being smaller than a fully grown man it possesses a relatively larger surface and therefore, as we shall see in considering animal heat, its metabolism is more rapid and it requires a relatively

larger amount of food on this account alone. During the first few months of life, milk is the only suitable food, and we have seen that human milk contains 2 per cent. proteid, 2·75 per cent. fat, and 5 per cent. sugar. In cows' milk the percentage of proteid is still higher; and the disproportion between proteid and carbohydrate in milk, as compared with the ordinary diet of the adult, as already given, is to be accounted for by the fact that the strain of growth, accompanied by the formation of new tissue, requires a larger relative amount of proteid in the food to meet it. For the infant, milk (human) is a *perfect food*, just as the egg is for the chick during incubation.

Effects of some constituents of the diet.—Alcohol appears to be partly excreted unchanged by the lungs and kidneys, but when taken in moderate amount some 95 per cent. of it is oxidised within the body. It thus appears to spare the oxidation of the fats, and in this way promotes the laying on of fat in those who have a natural tendency in this direction; but it is scarcely necessary to say that under ordinary circumstances alcohol is not taken as a food but as a stimulant. The ordinary individual escapes temporarily by means of alcohol from the burden of life, and as long as the problem before him remains the same, he will probably solve it in the same way. The most diverse opinions are held as to the value of alcohol for general use, but we cannot discuss the matter here.

It is to be noted that its stimulating effects are essentially temporary, and are followed by a sedative action, which, if the dose be sufficiently large, rapidly becomes depressant, and even toxic. Alcohol temporarily stimulates the nervous and circulatory systems, producing an increased flow of ideas, accompanied with a feeling of mental exhilaration and a quickening of the heart's action, with an increase in the strength of the beat and the fullness of the pulse. It dilates the peripheral blood-vessels and thus gives a subjective feeling of warmth to the body. It is to be noted, however, that the personal equation is a very strong element in the case of alcohol. An amount which will only harmlessly exhilarate one person is often sufficient to cause toxic effects in another. In fact, it is a useful and agreeable stimulant or a narcotic poison, not only according to the dose in which it may be taken, but also according to the susceptibility of the individual to whom it may be administered. Speaking generally, one to one-and-a-half fluid ounces of absolute alcohol in twenty-four hours is the most which a healthy man should take, whether in the form of spirits, wine or beer (Parkes).

"That alcohol taken in small quantities improves the appetite and beneficially increases the circulatory activity is almost universally admitted. Of its value as a sedative to the nervous system in certain diseased conditions there is also nearly a general acknowledgment; as to its influence on the work of the body—physical and mental—it would seem, when taken in the moderate quantity above stated, to be helpful under many circumstances. Taken in larger quantity it would seem, on the contrary, to be invariably hurtful; women seem more susceptible of its injurious effects than men, and should take it with even greater moderation, and healthy children should do without it altogether" (Burney Yeo).

We have only space here to refer to one or two other points of interest in the action of alcohol.

1. *Influence upon work.*—Alcohol does not of itself create energy. Its value in this direction, although it undergoes oxidation in the body, as do the other foodstuffs, may be regarded as *nil.* It enables the taker, however, to draw freely upon the energy which is already latent within him, especially upon the energy of the central nervous system. Under ordinary circumstances fatigue is nature's intimation that a man has withdrawn as much from his stock of energy as it is advisable he should do, and as his fatigue increases with further exertion, it becomes more and more difficult for him to continue depleting his exchequer. Alcohol has the effect of doing away with this natural economy; it removes for the time the feeling of fatigue and enables the man to reach his *reserve* stock of energy which under ordinary circumstances should not be touched. The animal frame possesses a valuable store of this reserve energy, and nature is ordinarily intensely jealous of its integrity. In the hour of need, as in severe illness, she will unlock her coffers and empty them to the last farthing when life itself is at stake, but in everyday life she does not want the reserve fund to be touched at all, and is at the best niggardly with it, however much we may entreat her. Alcohol offers a key to this store so jealously guarded by nature, a key which enables us to draw upon our reserve force almost as we will. It is scarcely necessary to say, however, that it is inadvisable in the extreme to take the control of our physiological finances out of nature's hands.

A consideration of this *modus operandi* of alcohol leads us to the conclusion, and the conclusion is verified by experience, that though of service to enable us to unlock our store of energy to meet a sudden strain, it is of no use, but only harmful, if a continuous strain has to be met. It is of no use to soldiers on the march or to others who are undertaking any prolonged

muscular exertion. On the other hand, when a strictly temporary effort is required, whether it be of the nature of a purely physical feat or the making of a parliamentary speech, and there is no need to consider the subsequent exhaustion resulting from the wasteful expenditure of energy, alcohol may be of considerable service. In other words, it may be of use as a spur, but this is the only sense in which it can be regarded as helpful.

With regard to mental work, alcohol is of no service whatever, in fact it is deleterious in the last degree. The student who, with his glass at his elbow, feels he is getting on swimmingly with his reading, will very soon learn his mistake by experience. He will subsequently find that his recollection of what he has read is by no means so distinct as when he studied under other conditions, and that many points which seemed plain at the time are by no means so afterwards. Alcohol appears to interfere very seriously with the process of *synesis* by which trains of thought become impressed upon the nerve-cells. We may regard the student reading upon alcohol somewhat in the light of a man trying to engrave upon butter, as contrasted with one engraving upon metal. In the former case the strokes are more easily cut than in the latter, but they are not so clearly defined and they readily fade away.

2. *Influence on temperature.*—Alcohol *reduces* the temperature by dilating the peripheral blood-vessels and so increasing the radiation of heat. At the same time, this peripheral dilatation induces a subjective feeling of warmth, which has given alcohol a reputation, ill deserved, for "keeping out the cold." As a matter of fact, it does no such thing, and a man exposed for any length of time to severe cold will succumb the sooner if he puts himself under the influence of alcohol. Indeed, its uselessness as a means of protection against cold is now so generally recognised, that a cabdriver of average intelligence will in the winter season very sensibly prefer to fortify himself with hot coffee; but *after* exposure to cold, incurred perhaps during a long drive, alcohol may be of the greatest service in increasing the circulation and dilating the peripheral arterioles, so that more hot blood reaches the extremities.

The following table shows the *strength* of some of the commoner alcoholic beverages—

Brandy	48	to	56	per cent.
Whisky	44	"	50	"
Rum and Gin	40	"	50	"
Port and Sherry	14	"	18	"
Champagne	10	"	13	"
Hock and Claret	8	"	11	"
Beer	3, 5, or more per cent.			

Beer, however, may vary very considerably in its strength, to such an extent indeed as from 1 to 10 per cent. According to Parkes, a pint of beer (20 ozs.) may be taken as containing on an average—

Alcohol	1 oz.
Extractives—Dextrin and Sugar	1·2 oz.
Free Acid (chiefly acetic, with small quantities of lactic, malic, and gallic acids)	25 grains.
Salts	13 grains.

Besides being a stimulant, beer has some value as a bitter tonic, which it derives from the hop extractives. The presence of carbo-hydrates, with a small amount of proteid matter, give it also a certain nutritive value, but the quantity required to afford the N and C required daily would amount to some 20 litres, a dose which would be altogether impossible, and indeed toxic, for most people.

Tea, coffee and **cocoa** also belong to the class of stimulants, but, unlike alcohol, they are not intoxicating, and people are thus less prone to take them to excess. Tea and coffee have a more powerful action than cocoa, an action they owe to the presence of the alkaloids *theine* and *caffeine*, which appear to be identical, while cocoa contains one closely allied to them—*theobromine.* Tea is characterised by the presence of a considerable quantity of tannin, coffee by that of various aromatic matters, while cocoa has a special nutritive value of its own, owing to the presence of sometimes as much as 50 per cent. of fat, with some 15 per cent. of proteid, and 5 to 15 per cent. of starch.

These substances, especially tea and coffee, act as true stimulants and restoratives of the nervous system, removing the sense of fatigue, clearing the mind, and promoting intellectual activity. They are admirable adjuvants to brain work of all kinds, and in this way afford a marked contrast to alcohol, to which they are in many ways antagonistic. Under ordinary circumstances they diminish the tendency to sleep, and may thus be regarded as anti-hypnotics. They are direct antidotes to the action of alcohol sometimes, especially coffee, and this is the *raison d'etre* of the usual post-prandial cup of this substance. The condition of mental inertia induced by a good dinner accompanied with wine is frequently completely dissipated by a small cup of strong coffee. It is to be noted, too, that it is customary to wash the stomach out with a hot infusion of coffee in cases of acute alcoholic poisoning. The superiority of coffee over tea as an antidote to alcohol is probably due in part at least to the belief that it contracts the intra-cranial blood-vessels instead of dilating them.

Tea should not be allowed to infuse for long before it is drunk, as, if so, in the cheaper kinds of Indian tea at least, a much larger quantity of tannin is dissolved out, and the infusion is more likely to cause dyspeptic trouble. The following table shows the result of an experiment by Dr Hale White with reference to this point. The teas infused were—(1) finest Assam, (2) finest China, and (3) common Congou, and the figures show the percentage of tannin yielded by each after short and long infusion—

	Percentage of Tannin.		
	(1)	(2)	(3)
Infusion for 3 minutes yielded........	11·30	7·77	9·37
" 15 " "	17·73	7·97	11–15

The figures speak for themselves. It will be seen that in the case of the more expensive China tea (2) the amount of tannin present is approximately the same, both for short and long infusion; while in the case of the cheaper Indian tea (1) the amount of tannin was half as much again when the infusion had lasted for fifteen minutes as when it had lasted for only three minutes, and in both cases largely exceeded the amount of tannin in the infusion of China tea. In many working-class homes, and it is here especially that the cheaper teas are used, it is quite a usual practice to make the tea as a matter of custom a considerable time before it is needed, and then to put the teapot on the hob or even into the oven in order to brew the tea. In this process of "brewing" or "mashing," not only the alkaloid theine is extracted, but practically all the tannin, and the resulting solution has a most deleterious effect upon the digestive apparatus. In the West of Ireland the drinking of brewed tea is said to constitute little less than a vice with the peasants, the teapot being placed on the peat sod on the hearth all day, and its black unhealthy contents constantly had recourse to. The wrecked digestion resulting helps on the nervous collapse provoked by the excessive amount of theine consumed, and even insanity is in some cases the ultimate result. The effects of the abuse of tea are of course not so marked as those of alcohol, and the abuse itself is not so widely spread. For both these reasons we do not hear very much of it, but that such abuse exists, and to an injurious extent, there can be no doubt; and it is to be

borne in mind that the evil of its abuse lies not only in the excessive amount of the stimulant consumed, but also, among the poorer classes at least, in the very injurious method of preparation.

We have already had occasion to refer to some extent to the effect of **inorganic salts** upon metabolism (page 511). The addition of a certain amount of sodium chloride to the food seems to be essential to the well-being of animals whose food is rich in potassium salts (Bunge). Now, most vegetables are rich in potassium salts, and it is consequently found that those races which consume them in large amount are particularly dependent upon the admixture of sodium chloride with their food; and the same is the case with many herbivorous animals, which often travel long distances to obtain it. On the other hand, the races of mankind which are flesh eaters, carnivorous animals, and those herbivora whose food does not contain an excess of potassium salts have not the same necessity.

The explanation of these facts, according to Bunge, lies in the presence of abundance of potassium salts in certain vegetable foods. If a salt of potash, such as the carbonate or phosphate, meets with sodium chloride in the blood, a double decomposition occurs, resulting in the formation of sodium carbonate or phosphate and potassium chloride, and these are excreted by the kidney, leaving the organism poorer in sodium and chlorine. In this way common salt is withdrawn from the body by the ingestion of potassium salts, and hence the need for common salt as an article of diet by those races and animals whose diet is rich in potassium salts. To a large extent of course common salt is taken by man merely as a condiment, just as mustard and pepper are taken.

CHAPTER XIV.

ANIMAL HEAT.

THE potential energy of the food, as we have seen, is converted by the metabolism of the body into the actual energy of mechanical work and heat. It is proposed in this section to consider the sources of heat and the mechanism regulating its production and loss.

Warm- and cold-blooded animals.—Birds and mammals possess a high temperature, which is in the main constant and independent of that of the surrounding medium, and they have for long been known as *warm-blooded* animals. Other animals much lower in the scale of evolution, such as amphibians, reptiles and fishes, have a much lower temperature, only slightly above that of the surrounding medium, and they are correspondingly known as *cold-blooded* animals. In marked contrast with mammals and birds, their temperature, so far from being maintained at a fairly constant level, varies directly with that of the medium in which they are placed. The essential difference in the two classes lies in the constancy and inconstancy of their temperatures, and they are hence more exactly known respectively as *homoio-thermic*, or animals with a constant temperature, and *poikilo-thermic*, or animals with a varying temperature. In other words, warm-blooded animals are distinguished from cold-blooded animals by their faculty of maintaining their normal temperature when exposed to cold or heat, instead of becoming either colder or hotter as the case may be. This power, we shall find, is due to the development in those animals which possess it of a "heat regulating mechanism," the nature of which we shall presently consider in some detail. Cold-blooded animals are without it, and their temperature consequently rises if the air or other medium in which they are placed becomes hotter, and falls if it becomes colder. Some animals, however, such as the marmot,

hedgehog, bat and dormouse, which hibernate in the winter, are at this time virtually poikilothermic or cold-blooded, while in the summer they are homoiothermic or warm-blooded. Moreover, the young of even typically warm-blooded animals, which are born in an immature and helpless state, are for a time in a condition in which they cannot maintain the temperature of the adult without artificial aid, such as the warmth of the parent's body, and so resemble for a period cold-blooded animals: so that while we use the terms warm-blooded and cold-blooded, or homoiothermic and poikilothermic, it is well to bear in mind that no very distinct line can be drawn between the two classes.

According to Edwards, if newly-born pups, kittens or rabbits are removed from their warm surroundings, their temperature falls till it reaches a point a few degrees above that of the air. On the other hand, he found that this was not the case with newly-born guinea-pigs, which could maintain their temperature if the cold they were exposed to was not too great. This is due to the fact that they are born in a condition of considerable development and activity, while the former animals are blind, helpless and, it may be, naked at birth. In this way the young of warm-blooded animals may be classified as warm-blooded or cold-blooded. Of course in a few days, the length of time varying in the case of different species, the fall in temperature of the cold-blooded young of warm-blooded animals upon exposure becomes less, and as their vigour becomes established they become more and more able to maintain their own temperature. Young birds may also be divided into two classes in the same way, those hatched without feathers and in a generally immature state reacting to changes in the external temperature like cold-blooded animals; while the chick, well covered with feathers and active and alert from the first, is warm-blooded to begin with. It is interesting to note that in the case of the chick the gradual development of the power of regulating its temperature has been observed. At one stage the embryo responds to changes in the external temperature like a cold-blooded animal; at a later stage it has acquired the power of regulation for moderate changes, and finally, when hatched, it has the powers of a warm-blooded animal in this respect.

[TABLE.

The following table shows the temperatures of various warm-blooded animals—

Animals.	Average Rectal Temperature.	Number of Observations.	Observer.
Horse	100·2° F.	On 212 horses.	Hobday.
Ox	101·9	On 352 cows and oxen.	Robertson.
Sheep	104·0	On more than 100 sheep.	Hobday.
Dog	101·5	On more than 200 dogs.	"
Cat	101·7	On 41 cats.	"
Rabbit	101·7	31 on 10 rabbits.	Pembrey.
Guinea-pig	100·2	19 on 5 guinea-pigs.	"
Rat	99·5	16 on 4 rats.	"
Mouse	99·3	27 on 8 mice.	"
Monkey	101·1	22 on 2 monkeys.	Hale, White and Washburn.
Echidna (Hystrix).	81·5	5 on 2 specimens.	Mikloucho Mac-lay.
	90·5	7 on 7 "	Semon.
Ornithorhynchus	76·6	2 on 1 "	Miklouche Mac-lay.
Fowl (common)	106·9	On 111 fowls.	Hobday.
	109·0	On 14 "	Davy.
Duck	107·8	On 24 ducks.	Hobday.
	110·5	On 8 "	Davy.
Goose	107·0	On 5 geese.	"
Pigeon	105·6	20 on 4 pigeons.	Corin and Van Beneden.
Ostrich	99·2	On 5 ostriches.	Hobday.

The above are the average results of several observations made by different observers. If we consider 98·4°F. to represent the normal temperature of man, it will be seen that it is lower than that of most of the mammals. The porcupine (echidna hystrix), however, shows a temperature in the one set of observations of 81·5, and in the other of 90·5; and the duck-billed platypus (ornithorhynchus) has a still lower temperature of 76·6. The temperature of birds is seen to be a few degrees higher than that of mammals.

The following table shows the temperature of various cold-blooded animals and the difference between it and their surroundings as recorded by various observers—

Animal.	Temperature of Animal.	Temperature of Surroundings.	Observer.
Viper	20°C. (68°F.)	14·4°C.	Hunter.
Python	24·4 (76)	15·6	Sclater.
Frog	17·2 (63)	16·7	Davy.
"	14·4 (58)	14·4	"
"	8·9 (48)	6·7	Czermach.
Shark	25 (77)	23·7	Davy.
Bonito	37·2 (99)	26·9	"
Crab	22·2 (72)	22·2	"
Leeches	13·9 (57)	13·3	Hunter.
Scarabæus	25 (77)	24·4	Davy.
Locust	22·2 (72·5)	16·7	"

The temperature of cold-blooded animals is generally a fraction of a degree above that of their surroundings, but there are exceptions to this, as shown in the cases of the python and bonito fish, in which the difference may amount to as much as 10 degrees.

Measurement of heat production.—1. *Calculation of heat production from diet.*—This may be regarded as an indirect method, and is, shortly, as follows:—The total energy of the body, given out in the form of mechanical work and heat, has for its primal source the chemical energy of the food. Now, the combustion value of the different foodstuffs, when these are burned in a calorimeter, has been accurately determined, and it is to be noted that though in the body the process of oxidation may be slower and proceed by stages, the energy given out by the complete combustion of a fixed quantity of any food substance is always the same. In the body the combustion of carbohydrates and fats is complete, while, as we have seen, that of the proteids is not, and an allowance must be made for the combustion value of the urea appearing in the urine, but to this we shall return later. The calculation lies in estimating the combustion value of the daily income of food, in other words in estimating the daily income of energy, and subtracting from it the daily expenditure in the form of mechanical work. The result gives us the daily expenditure in heat.

We may now proceed to make such a calculation as an illustration of the method. The following are given as the physical values of the three classes of foodstuffs as heat producers—

1 grm.	Proteid	white of egg (Frankland).....	4896	calories
		lean beef (Rubner)...........	5656	"
	Fat	....	9321	"
	Carbohydrate	....	4116	"

But from the physical value of the proteid must be deducted the heat value of the urea of the urine, which brings the average calorific value of the proteid of the aliment down to 4124 calories; and a further reduction is to be made for the escape of some of the products of combustion of the proteids in the fæces; so that the reduced or physiological heat value of 1 grm. of dry proteid may be estimated at about 4000 calories. If we translate gramme degrees to kilogramme degrees we find—

1 grm.	Dry proteid	=	4·0	kilocalories.
"	Fat....................	=	9·3	"
"	Carbohydrate.........	=	4·1	"

Applying these figures to Burden Sanderson's diet table we find that—

100	grms.	Proteid.......	×	4·0	=	400
100	"	Fat...........	×	9·3	=	930
250	"	Carbohydrate	×	4·1	=	1025
						2355 kilocalories

(or 2,355,000 calories).

We have now ascertained the physiological combustion value of the food taken, and it only remains to subtract from this the heat value of the mechanical work which has been done. An average day's work may be put at 150 kilogramme-metres—the equivalent of 351,000 calories of heat. Subtracting this from 2,355,000 we obtain 2,004,000 calories given off as heat per diem by a man engaged in light labour. This is a low estimate, and in the case of hard labour more food would be taken, and the calculation would work out at a much higher figure, say, 3,000,000 to 4,000,000 calories; and in cases of extreme exertion to a still higher figure.

Rubner, in calculating the production of heat in an animal by this method, has found the result to compare well with that of direct measurement of the heat given off in a calorimeter. Thus the food of a dog during twelve days was 228·06 grms. proteid, and 340·4 grms. fat. From this the following calculations were made—

Calculation 1.—From physiological heat values.

Proteid....	228·06	× 4·0 kilocalories	=	912·24
Fat.........	340·4	× 9·423 "	=	3207·0
				4119·24 kilocalories in 12 days.

Calculation 2.—From physical heat value, with reduction for heat value of urine and fæces.

Proteid	=	1222 kilocalories.	
Fat..................	=	3207 "	
		4429	
		305·2	{ 223·5 heat value of urine. 81·7 " " fæces.
Kilocalories in 12 days		4123·8	

The amount of heat given off by the dog during this time, as estimated by the calorimeter in which it was kept, was 3958 kilocalories, or 96 per cent. of the energy of the food.

2. *Measurement of heat production by calorimeter.*—This is a direct method in which the amount of heat given off is ascertained, and this necessarily corresponds to the amount of heat produced provided that the animal itself maintains a constant temperature. Various forms of calorimeter have been employed, *e.g.*, the ice calorimeter of Lavoisier and Laplace, in which the amount of heat given off is measured by the amount of ice liquefied. Following this was the water calorimeters of M'Kendrick and others, in which the heat given off is estimated by the rise in temperature of the water employed. This calorimeter had advantages over the first, but neither of them are suitable for accurate experiments upon animal heat. The calorimeter now chiefly used is the air one of Haldane, Hale White and Washburn. The air calorimeter comprises two similar chambers, each of which has two walls of

thin sheet copper, between which is an air space. The outer wall is covered externally by a layer of felt to prevent variations in the temperature of the surrounding air from draughts affecting the temperature of the air in the air spaces of the two chambers between the copper sheets. The air spaces communicate with the two limbs of a manometer, which serves as a differential thermometer, for through it the heat given off by an animal in one of the chambers may be balanced by the heat given off by a hydrogen flame in the other. The heat given off by the animal in its chamber causes a rise in the temperature of the air in the copper jacket and increases thereby its pressure upon the fluid in the manometer and thus tends to move it towards the other chamber. This tendency is counteracted by the heating and consequent rise in pressure of the air in the jacket of the other chamber by the hydrogen flame, which is turned up and down during the experiment until the fluid in the manometer remains level in the two limbs. The amount of hydrogen burned is estimated by the amount of water formed, and the heat of combustion of hydrogen being known, the heat given off by the flame is readily calculated; and this is necessarily the same as the amount of heat given off by the animal when the fluid in the manometer is evenly balanced. A special advantage of this form of calorimeter lies in the fact that the loss of heat by conduction and radiation from the chamber containing the animal is compensated by a similar loss from the chamber containing the hydrogen flame.

Air is led through the two chambers by tubes, care being taken that the ventilation is the same in each case. The calorimeter may be so arranged as to act as a respiratory apparatus, and the intake of oxygen and output of CO_2 be thus ascertained. As the respiratory exchange is a measure of the combustion taking place in the tissues, it forms a measure of the heat produced, and may be used to check the calorimetric reading.

3. *Measurement of heat production by respiratory exchange.*—When a warm-blooded animal is exposed to a cold medium, the output of CO_2 and intake of oxygen are increased; when it is exposed to an increase in the temperature of the surrounding medium, the output of CO_2 and intake of oxygen are diminished; and in either case, under ordinary circumstances, the animal's temperature remains the same. In other words, the heat production varies inversely with the temperature of the surrounding medium, and the record of the alterations in the respiratory exchange is thus of the greatest value in studying the regulation

of temperature by heat production. In many ways the respiratory exchange affords a more convenient method of estimating the heat production than the calorimeter, owing to the time, trouble and possible sources of error involved in the use of the latter.

Seats of heat production—heat loss.—As metabolism is going on to a greater or lesser extent in all the tissues, heat is produced to some extent in every part of the body. The *muscles*, however, produce a very large proportion of the heat, and after them, though at a considerable distance, come the *glands*, and then the *central nervous system* as heat producers. As we have already seen, the relation of heat to work as a result of muscular contraction is very variable. We have seen that the work done by an excised frog's muscle may rise to one-fifth of the total chemical energy expended, and sink as low as $\frac{1}{25}$. And though the unexcised mammalian muscle works more economically, and under favourable conditions as much as one-third of the chemical energy expended may appear as work, a very considerable proportion remains to be accounted for as heat. During severe labour the amount of heat given out by the muscles is greatly increased, a fact that is readily brought home to us all; but it must not be overlooked that even during rest the muscles, though their metabolism is less active, are still producing heat. We shall have further occasion to consider this phase of their activity when we deal with the mechanism regulating the production of heat. In the meantime we may note that the muscles constitute the most important thermogenic tissue in the body, and that their function in this respect is carried on entirely independently of contraction, though this, when it takes place, increases the amount of heat produced.

After the muscles, the various glands take rank as heat producers. In the case of the submaxillary gland of the dog, Ludwig found that the temperature of the saliva secreted during stimulation of the chorda was 1 to 1·5° above that of the blood in the carotid artery. It is, however, to be noted that the increased blood-supply to the glands during their activity will itself lead to an increase in their temperature which may mask the heat produced by the gland tissue itself. Bayliss and Hill, after investigating the production of heat in salivary glands, conclude that the temperature of the saliva on stimulating the chorda never rises higher than that of the aortic blood. No doubt the gland produces more heat while it is actively secreting, but owing to its small size and the rapidity of the circulation of blood through it, the difference in the heat production by the gland tissue itself cannot be shown. The liver, however, is of much more importance

as a heat producer than the other glands, not only because of its large size but also because it is in a state of constant activity. A very large amount of heat must be set free in the course of the various metabolic changes taking place in it, though some allowance should doubtless be made on account of such of these as are synthetical (*e.g.*, the conversion of carbonate of ammonia to urea), and therefore result in the absorption and not in the setting free of heat. When, however, allowance has been made for these, there must still be a large amount of heat set free to be reckoned with; and Bernard found the liver to be the hottest part of the body, and that the blood of the hepatic vein was higher in temperature than that of the portal, especially during digestion; indeed, the blood in this vessel is said to be of a higher temperature than that in any other part of the body, *e.g.*, than that of the aorta or vena cava inferior.

The brain also cannot be denied a place as a heat producer, for thermometers inserted into its tissue record a higher temperature than that of the arterial blood supplying it; but its importance in this respect must be very much less indeed than that of the muscles and glands.

Heat loss.—Heat is lost to the body (1) from the *skin* by radiation, conduction and evaporation of water of perspiration; (2) from the lungs by the heating of the expired air and evaporation of water of respiration; (3) in the warming of the fæces and the urine. Stewart gives the following as an approximate analysis of the heat loss of an average man—

		Per cent.		Calories.
Skin	Evaporation of water	15	80	400,000
	Radiation	30		750,000
	Conduction (and convection)	35		900,000
Lungs	Evaporation of water	15	17·5	400,000
	Heating the expired air	2·5		70,000
	Heating the excreta		2·5	70,000
			100	2,590,000

The skin and lungs therefore afford the chief means of the loss of heat from the body, and of these the skin is undoubtedly the most important in regulating the loss.

Regulation of Temperature in Warm-blooded Animals.

The normal temperature of man, as we have seen, is about 98·6°F. or 37°C., and this temperature, like that of other warm-blooded

or homoiothermic animals, is under ordinary circumstances maintained with but very slight variations, whatever—within certain limits—the changes in the temperature of the surrounding medium, or in the amount of heat produced in the body itself, may be. This maintenance of a mean temperature is attained by a mechanism of adjustment between the heat produced in the body and the heat lost from it. Thus when the conditions are such that the bodily temperature would otherwise rise, the normal temperature may be maintained (1) by an increased loss of heat or (2) by a diminished production; and, similarly, when the temperature would otherwise fall, the normal temperature may be maintained (1) by a diminished loss of heat or (2) by an increased production.

Regulation by variations in loss of heat.—We have already seen that the two chief means whereby heat is lost from the body are afforded by the lungs and the skin; and of these two means of loss in man the latter is by far the most important in regulating the temperature. But though in man the respiratory tract thus plays a subordinate part in regulating the temperature, it is to be noted that the importance of this means of regulation varies greatly in different animals. Thus the dog covered with a thick coat of fur, and perspiring little if at all from the general skin surface, makes use of respiration as a means of increasing its loss of heat to the utmost extent, and when "over-heated" pants rapidly with extended and lolling tongue. In such animals, as contrasted with man, the loss of heat from the body is varied by respiratory rather than by cutaneous changes. The changes are effected not in the pulmonary alveoli, but in the more superficial portions of the respiratory tract—the nose, the pharynx and to some extent the larger bronchial tubes.

In man, however, the loss of heat is for the most part regulated through the skin surface, and it is regulated in two ways—(1) by vaso-motor changes, (2) by the action of the sweat glands. Thus if the cutaneous vessels are dilated, more hot blood passes through the skin and more heat is lost by conduction and radiation; while, conversely, if the vessels are constricted, less heat is lost in this way, as the blood is driven into the deeper parts of the body. Again, when perspiration takes place heat is lost by evaporation; while this source of loss ceases when the activity of the glands is again restricted. The part played by the skin in these ways is well seen in the case of ordinary muscular exercise. The contraction of the muscles increases the production of heat in the body, and were this increased production not compensated for by a corresponding loss, the temperature of the body would rise

considerably, whereas it is increased but slightly or not at all. Some of the heat produced is lost by the quickening of the respiration, but the main loss takes place through the skin, owing to the dilatation of the cutaneous vessels and the evaporation of the increased perspiration. Again, if the body be exposed to external cold, the action of the skin in regulating the loss is again illustrated. The cutaneous vessels become constricted, the blood is sent into the deeper parts of the body and less heat is lost by conduction and radiation. Under the opposite influence of exposure to external warmth, the cutaneous vessels become dilated, more heat being thus lost by conduction and radiation, and the sweat glands secrete freely, leading, under favourable circumstances, to still further loss of heat by evaporation.

The loss of heat from the skin surface which might otherwise be excessive, *i.e.*, more than could be compensated for by increased production of heat and constriction of the cutaneous vessels, is restricted in various ways. Man voluntarily adopts means to diminish it by wearing clothes, and other warm-blooded animals are protected by a layer of fur or feathers, or, as in the case of the whale, seal and walrus, by a thick layer of subcutaneous fat. Clothes, fur and feathers diminish the loss of heat by enclosing strata of more or less stationary warm air, which forms a bad conductor of heat. In this connection it is to be noted that it is a common experience that a lower external temperature may be borne with comfort when the air is stationary than when there is a wind.

The size of the body has an important relation to the loss of heat from the skin surface, and also, as we shall see, to the rate of metabolism and the consequent production of heat. The larger the animal the greater is its weight or volume in proportion to its surface, for whereas weight or volume increases as the cube, surface increases as the square. If the dimensions of a body be increased from one to two, whereas the surface increases from one to four, the cubic content increases from one to eight. The smaller the animal, therefore, the greater surface in proportion to weight or volume is exposed, and a correspondingly greater proportionate loss of heat will take place from it, other conditions being the same. But small animals maintain their temperature as do large ones, and this is effected both by special means for economising the loss of heat from the skin surface and by a greater production of heat in proportion to their size. Thus a mouse has a relatively thicker covering of hair than a horse, the loss of heat by radiation and conduction from its skin surface being thus proportionately diminished and its metabolism and

consequent heat production is at a higher level, necessitating a proportionately larger supply of food. Indeed, as common observation shows, the larger supply of food required in proportion to their size is quite a characteristic of the smaller animals, and it is intimately related to the maintenance of their temperature. Thus we see that the metabolism of an animal varies as its surface and not as its mass.

With regard to the loss of heat by evaporation, we have used the words "under favourable circumstances," and it is to be noted that the efficiency of the secretion of sweat as a means of increasing the heat loss depends upon the dryness of the surrounding air. In experiments on the effect of extreme heat upon the body, it was found that when the air was moist the temperature rose, whereas it remained normal when the surrounding air was at a temperature of 126°F., provided it was dry. These experiments illustrate what is indeed found to be the case, that a much higher temperature can be borne in dry air than in one saturated with moisture. In dry air the water of perspiration readily evaporates and cools the skin, while in moist air the evaporation of water takes place much less readily; and in air saturated with watery vapour at the temperature of the body no loss of heat by evaporation of perspiration or from the respiratory surface can take place. In a saturated atmosphere at a temperature of 35° to 40°C. the temperature of an animal soon rises and death ensues. This is due to the fact that the regulation of the temperature in a warmer atmosphere than normal is secured by an increase in the loss of heat rather than by a decrease in its production. Evaporation from the skin and lungs is as important in checking overheating as increased production of heat is in checking excessive cooling. Hence when evaporation becomes no longer possible, the means for regulation are no longer adequate, the temperature rises, and the animal succumbs.

Regulation by variations in production of heat.—The normal temperature of the body is maintained not only by variations in the loss of heat, but also by variations in the production, through a mechanism which is under the control of the nervous system. Apart, however, from this mechanism, to the consideration of which we are about to turn, certain other circumstances, to which we have at different times already had occasion to refer, have an important relation to the amount of heat produced. As we have already seen, the smaller the animal the greater is the proportion of skin surface to mass or volume; and the greater in consequence is the production of heat per unit of mass to compensate for the

greater proportionate loss by radiation and conduction. Again, food has the effect we should expect in temporarily increasing the metabolism, and thus the production of heat; in the case of a dog, the production at the ninth hour after a meal being found in certain experiments to be 20 to 25 per cent. greater than before food was administered or after the animal had returned to its usual level of metabolism. Muscular exercise, too, is an important factor in the production of heat, the greater the amount of muscular contraction, the greater being the amount of heat produced. Finally, not only does the rate of heat production vary in different kinds of animals, even when of the same weight and volume, but animals of the same species have their own co-efficient of heat production, for, as we have already had occasion to point out, there is always the personal equation of metabolism to be reckoned with.

Having mentioned these causes of variation in the amount of heat produced, some of which are voluntary or accidental, we may now turn our attention more particularly to the special thermogenic mechanism to which we have just referred, whereby the production of heat is constantly varied and the temperature of the body maintained at its normal level. If a frog or other poikilothermic animal be exposed to increased external warmth, its temperature rises, and, as we should expect, the consumption of oxygen and evolution of CO_2 is also increased—in other words, there is increased respiratory exchange. If the animal be exposed to a lower temperature, on the other hand, its own temperature falls, together with its respiratory exchange. Thus heat increases and cold diminishes the metabolic activity of the tissues of a cold-blooded animal; the tissues acting like a mixture of non-living chemical substances, the interaction of which is favoured by heat and retarded by cold. Now, it is not so with warm-blooded animals: if one of these be exposed to a lower external temperature, the respiratory exchange is increased, indicating an increased metabolism and production of heat; while the temperature of the body remains the same as before. Exposure to a higher temperature has the effect of decreasing the metabolic processes and production of heat, but it must be borne in mind that the influence of heat in this respect is much less marked than that of cold. As we have already pointed out, the warm-blooded animal in a hot atmosphere relies more upon its capacity for increasing its loss of heat from the skin and lungs for the maintenance of its normal temperature than upon any reduction of the heat produced.

This power of the warm-blooded animal to so react to changes in the external temperature lies in the neuro-muscular apparatus,

a fact which is demonstrated by the following well known experiments. If such an animal be poisoned with curara, it is found that its temperature and respiratory exchange fall, and it subsequently responds to changes in the temperature of the surrounding medium precisely as a cold-blooded animal does. That is to say, exposure to warmth increases its temperature and respiratory exchange, while exposure to cold has the reverse effect. The explanation of this is that curara paralyses the motor nerve endings, thus cutting the muscles off from impulses which would otherwise reach them from the central nervous system. Cold and heat appear to produce their effect on the metabolism and heat production in the muscles of a warm-blooded animal reflexly, the path being—skin, afferent nerve, spinal cord, brain, spinal cord, motor nerve, muscle; and thus when the animal is curarised the reflex chain is broken in the region of the motor end-plates. We should expect that interruption of the reflex arc at other points would have the same effect, and this is practically found to be the case. Section of the spinal cord in the lower cervical region induces a fall in the temperature of the animal, and though some of this is due to loss of heat by vaso-motor paralysis of the vessels of the skin, part of it is due to a diminution in the metabolism and heat production of the paralysed muscles. When an animal that has been so treated is exposed to changes in temperature in the surrounding medium, it is found, like the curarised animal, to have lost its power of normal reaction, and to respond to the changes in the same way as the frog.

Heat centres.—We cannot as yet speak definitely as to the precise nature of the influence exerted by the central nervous system on the heat production of the body. It has been supposed that there are certain "heat centres" in the brain which are concerned with the regulation of the metabolism of the tissues, especially of the muscles, and so of the heat production; these centres causing increased metabolism when the temperature of the body would otherwise fall, and decreased metabolism when it would otherwise rise. Experiments in the way of injuries to different parts of the central nervous system by puncture have resulted in an increased production of heat, as shown by increased metabolism and increased respiratory exchange, as well as by direct calorimetric measurement. Thus Aronsohn and Sachs found that in rabbits, while puncture of the front part of the cerebral hemispheres had no effect, if the puncture was made through the middle part of the corpus striatum the result was a rise of temperature in a few hours which lasted for a few days. A similar rise could also be produced by electrical stimulation of

the corpus striatum. Hale White found that injury of the optic thalamus had a similar effect. In these cases the effect is no doubt due to stimulation of the parts in the immediate neighbourhood of the injury. But instructive as these and many other experiments of a similar nature may be, it is impossible to say that the existence of special heat centres in the brain has been definitely proved. The matter is to be regarded at present as *sub judice*, and all we can say with any certainty is that lesions of certain parts of the brain do result in increased heat production without inducing any other very obvious effect.

Effect of extremes of heat and cold.—Efficient as the mechanism for the maintenance of the normal temperature may be under ordinary circumstances, it must be borne in mind that it is only operative within certain limits. If the temperature of the surrounding medium be either raised or lowered to a sufficient degree the mechanism ceases to be adequate to the strain placed upon it, the normal temperature is no longer maintained, and the animal succumbs. It is readily understandable that the loss of heat may become so great that the increase of heat produced is unable to keep pace with it. When this happens, the temperature of the animal will necessarily fall and it will die of cold. This, as we have seen, is what occurs when the loss of heat from the skin surface of a rabbit or guinea-pig is increased by varnishing the skin or shaving it. In this case, unless the air of the chamber be raised in temperature to check the excessive loss of heat, or the animal be allowed to shelter itself in some warmer nook, the temperature of the body steadily falls and death ensues. When the loss of heat is sufficiently increased, either by lowering the external temperature or depriving the animal of its protective covering, as in the case instanced, and the heat regulating mechanism breaks down, the metabolism of the tissues generally is lowered, there is a slowing both of the anabolic and katabolic changes. The parts of the brain concerned in consciousness have their activity markedly affected, and the general depression may pass insensibly into the sleep of death, as in the case of those overtaken in the snow.

On the other hand, when the external temperature is raised to such an extent that the loss of heat from the lungs and skin is unable to compensate for it, the temperature of the body rises, together with the metabolism of the tissues generally. The heart and respiratory centre are excited and overworked, and the central nervous system sharing in the general disorder death frequently results from convulsions, or is preceded by simple

coma. But the temperature of the body may be raised to a degree incompatible with life, *i.e.*, some six or seven above the normal, not only by a rise in the temperature of the surrounding medium, but, as in **fever**, by too great a production of heat in the body itself and an accompanying breakdown in the mechanism securing a compensating loss. An increase in the heat production alone, without an accompanying derangement of the regulating mechanism as a whole, would not result in the high temperature of fever, for muscular exertion increases the metabolism as much or more, but the rise in temperature caused by it is much less, and the normal temperature is rapidly regained when the work is over. That there is increased production of heat in fever, as shown by increase in the metabolic changes, is indicated by the increase in the respiratory exchange and urea eliminated. Direct calorimetric observations also show an increase in the heat produced.

Diurnal and other variations in the temperature.—The ordinary temperature of man is 37°C., but it may show variations in health between 36° and 38°. There is a *diurnal variation*, the lowest temperature (36·3°) occurring between two and six o'clock in the morning, and the highest (37·5°) between five and nine in the evening. Similar variations occur in cases of fever, though they are generally greater in extent. *Food* also causes a slight increase in temperature, which does not, however, in health, exceed half a degree. *Age* and *sex* have some influence. In the young and old the mean temperature is somewhat higher than in vigorous adult life, and it is to be noted, too, that the heat regulating mechanism is not so perfect and more liable to accidental derangement. The temperature of women is said to be a little higher than that of men, and more susceptible of change. Sometimes a *post-mortem* rise in temperature is observed, especially after certain diseases, such as tetanus. The cause of the rise appears to lie in the continued metabolism of the tissues, while the loss of heat is checked by stoppage of the circulation. The onset of rigor mortis may be marked by a considerable accession of heat.

CHAPTER XV.

THE SENSES.

THROUGH the senses the mind receives impressions from the outer world, and these impressions, or sensations as they are called (consciousness being involved), form the basis of various mental processes, such as memory, pleasure, purpose, &c.

For the production of sensation the following mechanism is required—(1) Nerve terminations to be affected by the stimulus; (2) afferent nerve-fibres to form a conducting path to the brain; and (3) a central organ in the brain to receive and "elaborate" the transmitted impulse.

The peripheral nerve terminations receiving the impulse from without vary in the degree of their complexity from the simple plexuses of nerve-fibrils with their endings in the epidermis of the skin concerned with *general sensibility* to the highly developed end-organs of *special sense*, such as are found in the organ of Corti in the membranous labyrinth of the ear and in the retina of the eye. In the latter types the end-organ is represented by "nerve-epithelium," as it may be called, consisting of a special development of the epiblastic epithelial layer at some particular point or circumscribed area at which the nerve of special sense reaches the periphery. Thus in the retina (which is really an outgrowth from the brain) we have the *rods* and *cones*, both parts of modified epithelial cells connected by their central ends with nerve-fibrils of the optic nerve; and in the ear, the *hair-cells of Corti* in physiological continuity with fibrils derived from the auditory nerve. And it may be noted here, that whereas in the case of general sensibility, in which the fibrillar terminations in the epithelium of the skin are concerned, as already mentioned, the peripheral receiving mechanism is comparatively simple and scattered over a wide area, in the case of the special senses, such as those of hearing and seeing, it is definitely localised and circumscribed and conspicuously complex. In other words, the more general the sense, the more simple and more widely diffused is the receiving apparatus; while the more highly specialised the sense becomes, the more limited is the area of its distribution

—the more localised—and the more complex in structure is found the peripheral end-organ. The senses of touch, pressure and temperature are the most widely spread; those of hearing, seeing, smelling and tasting the least.

But whether at first sight simple or complicated in structure, all the organs of sense present contain fundamental characteristics —they all possess specially modified cells, or the processes of such cells, to receive the impressions from without, though, as in the case of the skin, the condition may be somewhat masked. The olfactory membrane may be taken as illustrative of the typical arrangement, which obtains also in the skin of certain annelids, such as the earthworm. The olfactory nerve- or sense-cell reaches to the free surface, being supported and surrounded by columnar epithelial cells. The afferent nerve-fibrils are direct continuations of the central ends of the olfactory cells, passing in the olfactory nerve to the centre in the brain, where they become interlaced with the processes of the nerve-cells in the centre, as shown in Fig. 301.

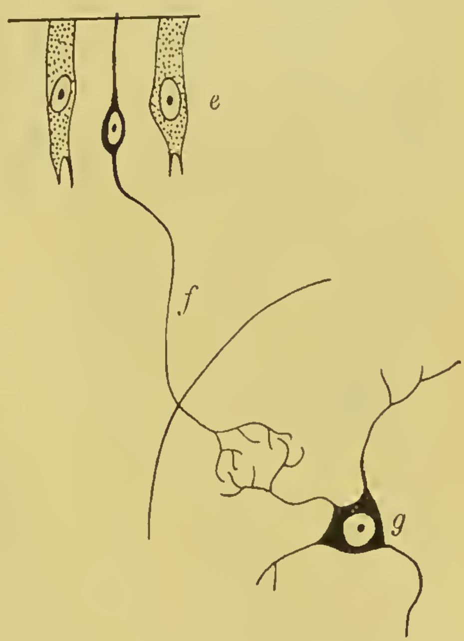

Fig. 301.—Diagram of Sensory Nerve-Fibres of Olfactory Epithelium and Bulb.

e, Epithelial cell (columnar); *f*, sensory nerve-fibre connected above with sensory nerve-cell, and passing below to centre in bulb *g*.

In the earthworm a similar arrangement is found in the skin. Here spindle-shaped cells occur scattered throughout the epithelium, their peripheral processes extending to the surface, and their central ones passing as nerve-fibrils through the tissues to the nerve centre. In another annelid (Nereis) we find that only the peripheral process of the sense- or nerve-cell extends to the surface between the epithelial cells, the body of the cell itself lying more deeply, entirely beneath the epithelial layer. And thus we have a link between the typical condition, as seen in the olfactory membrane and in the skin of the earthworm, and what we find in the case of the vertebrate skin. In the latter, the sense- or nerve-cell has been still further withdrawn from the surface epithelium—to

wit, as far as the ganglion on the posterior root of a spinal nerve. The accompanying figure represents these three stages diagrammatically.

It is not quite certain, however, how we are to regard the arrangement of parts in the other organs of special sense from this point of view.

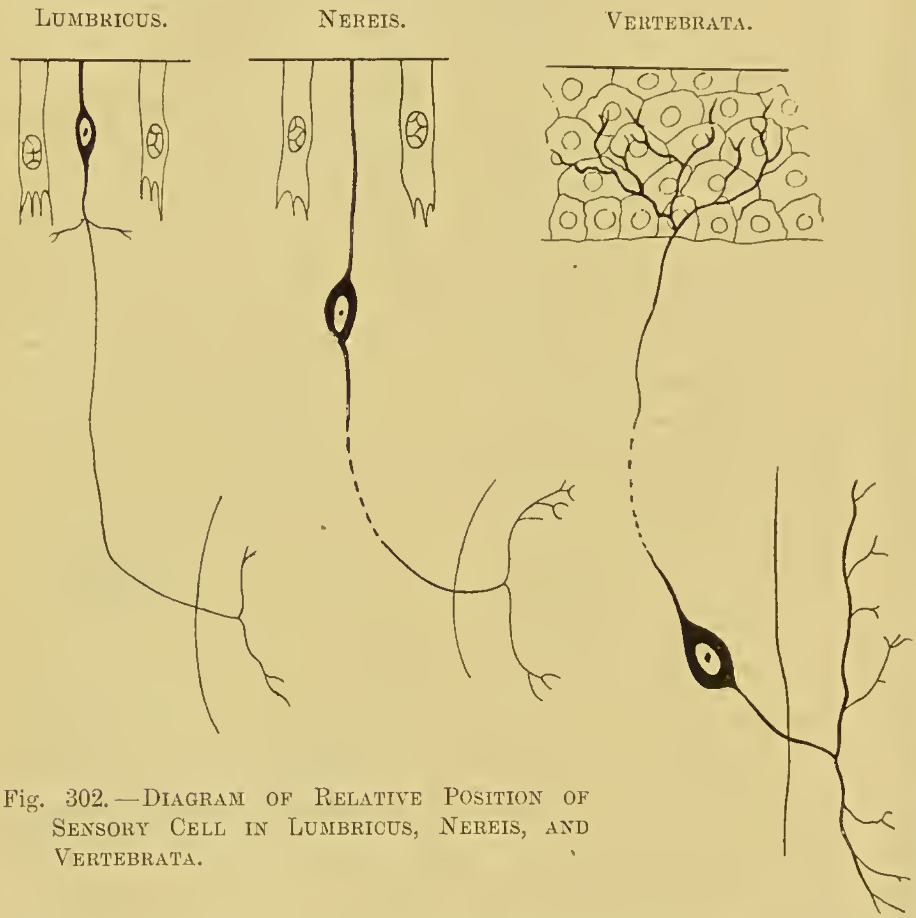

Fig. 302.—DIAGRAM OF RELATIVE POSITION OF SENSORY CELL IN LUMBRICUS, NEREIS, AND VERTEBRATA.

In the organ of Corti in the ear, the *hair-cells* possess no central process, and it may be that they exercise only a mechanical effect on the arborescent terminations of the auditory nerve-fibres which embrace their rounded bases; in which case the terminal sense cells might be looked for in the spiral ganglion, the fibrils between this and the hair-cells being their peripheral processes.

It used to be thought that the gustatory cells were prolonged at their central ends into a nerve-fibril, and this would bring

them into correspondence with the olfactory cells. The later view, however, that no such prolongation occurs, and that they are not in direct continuity with the fibres of the glosso-pharyngeal nerve, would make the arrangement more analogous to that of the auditory apparatus and integument.

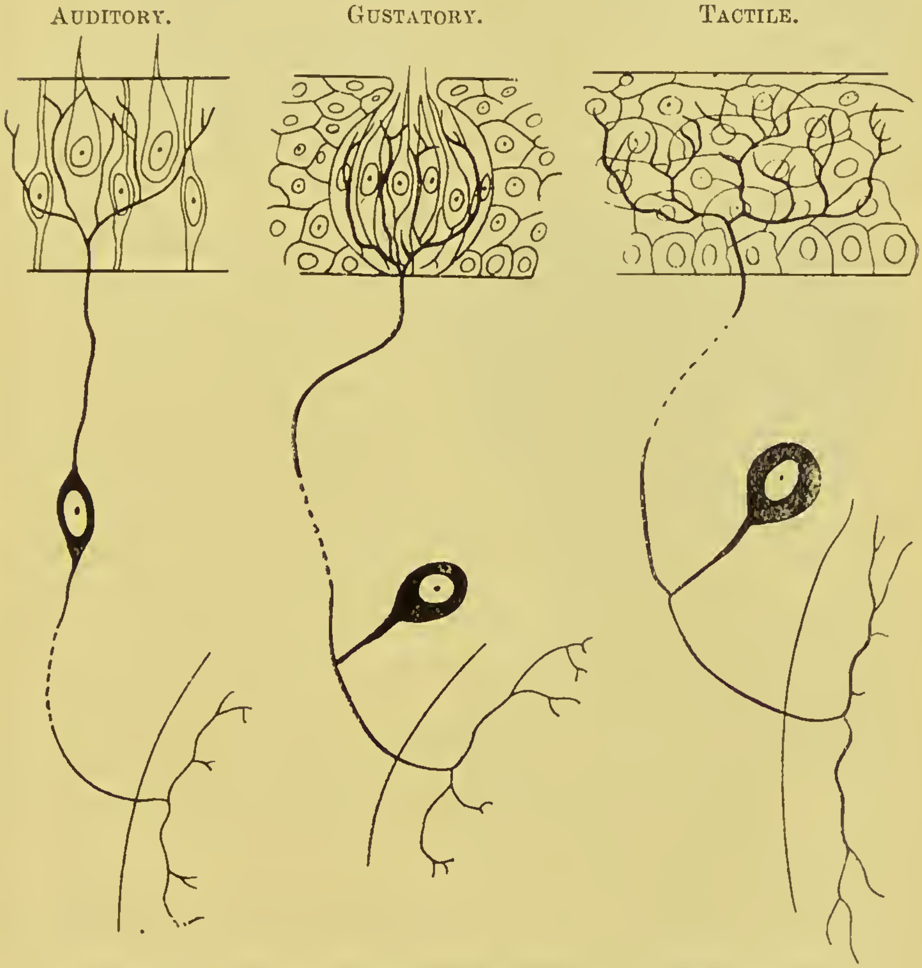

Fig. 303.—DIAGRAM SHOWING TERMINATION OF SENSORY NERVE-FIBRES IN AUDITORY, GUSTATORY, AND TACTILE STRUCTURES OF VERTEBRATA.

In the case of the retina, which is an outgrowth from the brain and not a direct development of the peripheral epithelium, it is still more difficult to speak with certainty. We may consider the *rod-* and *cone-cells* the homologues of the olfactory cells, or we may regard the bipolar cells of the inner nuclear layer in this light. We must not, however, pursue the subject further here.

As we should expect, organs differing so much in their anatomical distribution and structure as those of the senses, differ also in the kind of stimulus to which they are most susceptible. These *homologous stimuli* may be divided into—(1) Vibrations set up at a distance from the receiving mechanism, such as light and radiant heat, and (2) actual contact of the stimulating body with the sense organ, such as occurs in the case of touch, taste, smell, and hearing; for the olfactory cells are stimulated by odoriferous particles carried into the nostrils by the air, and the organ of Corti in the ear by movements of the endolymph transmitted through the ossicles from the membranum tympanum and outside air.

Thus each sense has its *adequate* or *homologous stimulus*, the retina being suited to receive rays of light, the olfactory membrane odoriferous particles, the gustatory cells substances in solution, the sense of touch ordinary contact, and so on. But, at the same time, they are not immune of necessity to the influence of stimuli which are not homologous. Thus a blow on the eyeball, or even pressure on it with the finger, will stimulate the retina, producing a sensation of light, stimulation of the tongue with electricity a sense of taste, and buzzing in the ear may result from an accumulation of wax in the external auditory meatus.

Sensations are referred by the brain to the area of distribution of the nerve stimulated, though the consciousness of the sensation necessarily takes place in the brain itself. Thus, when the finger is injured, the pain, though occurring really in the central nervous system, is *felt* in the finger itself, and this reference of the sensation to the area of distribution of the stimulated nerve occurs even when the nerve is stimulated at some part of its course. Thus a knock on the elbow stimulating the ulnar nerve may cause pain in the fingers, and stimulation of the stump of an amputated leg pain in the toes.

A sensation lasts longer than the stimulus which causes it, and these *after-sensations*, as they are termed, are of some interest in the case of retinal stimulation, under which they are more fully referred to (see "After-images").

Subjective sensations are those which are not the result of stimulation of the sense organs from the outside, but which have their origin in the cerebral centres themselves. Ordinary hallucinations of sight and hearing are of this nature.

By *anæsthesia* is meant a diminution or disappearance, and by *hyperæsthesia* an increase, of sensibility. And these conditions may result from changes at the periphery or the centre, or in the conducting medium between them. Thus blindness may be caused

by changes in the retina, in the optic nerve, or in the centre for sight in the brain.

The *intensity* of a sensation depends, as we might infer, upon the strength and duration of the stimulus and the excitability of the sensory apparatus. A minimal stimulus, *i.e.*, the smallest one producing an effect, indicates the *minimum limit of excitation;* when the stimulus is so strong that the mind cannot appreciate any increase in its strength, the *maximum limit of excitation* has been reached. Most of our sensations lie somewhere midway between the two extremes. We may now consider the senses in greater detail.

The Eye and Vision.

Structure of the eye.—The outermost coat of the eyeball—the **sclerotic**—is thick, tough and elastic, and affords support and protection to the structures enclosed within it. It consists of a dense feltwork of bundles of white fibres which run some in the sagittal line, *i.e.*, longitudinally, and others at right angles to these. There are to be found between the bundles of fibres the usual connective tissue cells (some of them pigmented), lymph spaces, and a few blood-vessels. The sclerotic coat extends over the posterior five-sixths of the eye, the remaining sixth being completed by the *cornea* in front, while behind the sclerotic is continuous with the dura mater investing the optic nerve. Whereas the sclerotic is opaque and white, the cornea is translucent and colourless, and forms a segment of a smaller sphere than the rest of the eyeball. It is composed of a number of superimposed lamellæ of white fibrous connective tissue, between which are found the corneal corpuscles—nucleated branched cells flattened conformably with the surfaces of the lamella between which they lie, the branches of one cell anastomosing chiefly with those of its neighbours in the same plane. Covering the surface anteriorly

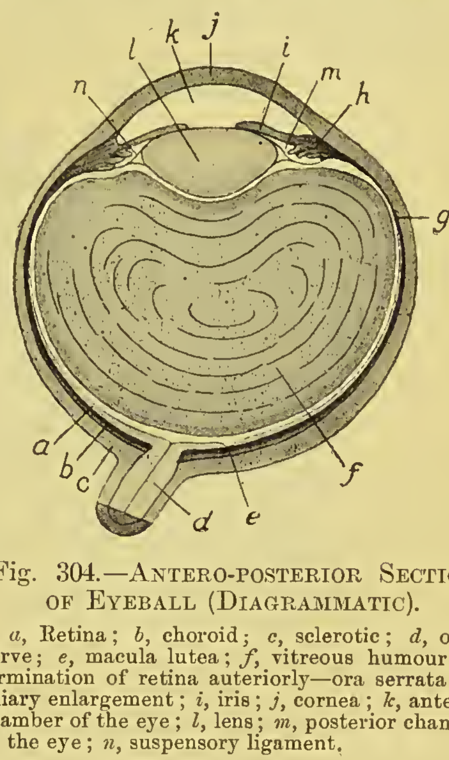

Fig. 304.—Antero-posterior Section of Eyeball (Diagrammatic).

a, Retina; *b*, choroid; *c*, sclerotic; *d*, optic nerve; *e*, macula lutea; *f*, vitreous humour; *g*, termination of retina auteriorly—ora serrata; *h*, ciliary enlargement; *i*, iris; *j*, cornea; *k*, anterior chamber of the eye; *l*, lens; *m*, posterior chamber of the eye; *n*, suspensory ligament.

is a layer of stratified squamous epithelium resting on a basement membrane, and continuous at the margin of the cornea with the epithelium of the conjunctiva. Posteriorly the body of the cornea is covered by a very distinct elastic membrane of considerable thickness, the *posterior elastic lamina* of Descemet, which in its turn is covered by a single layer of flattened epithelial cells continuous at the corneal margin with those lining the rest of the anterior chamber of the eye. The *conjunctiva* extends upon the surface of the sclerotic (Fig. 307) from the periphery

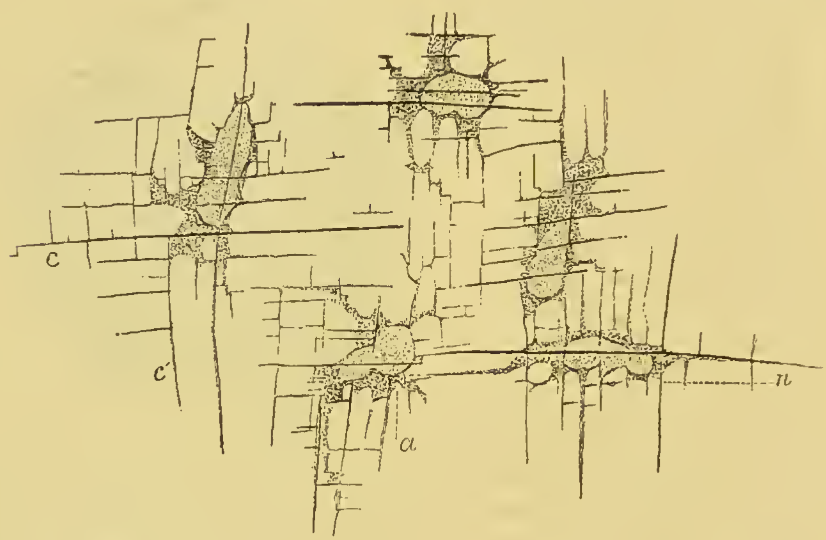

Fig. 305.—Corpuscles and Nerve-Fibrils of Cornea of Frog (Gold Chloride Preparation).

n, Nerve-fibril; *c*, terminal fibrils; *a*, corneal corpuscle.

of the cornea till it is reflected upon the inner surface of the eyelids as the palpebral layer, which meets the general integument at their edges. It consists of a somewhat thin layer of stratified squamous epithelium resting upon a basis of somewhat loose connective tissue, but only the epithelium is continued over the cornea, of which it forms the anterior epithelial layer already referred to. The cornea is liberally supplied with nerves derived from the long ciliary. The nerve-fibrils run in all directions, forming a well-marked plexus beneath the anterior epithelial layer, from which delicate filaments pass between the epithelial cells to form an intra-epithelial network. Many of the fibrillæ are beaded or varicose. The cornea is extra-vascular, that is to say, no blood-vessels penetrate it, and it

is nourished by the percolation of lymph through its inter-communicating system of cell spaces. It possesses no lymphatic vessels proper.

The middle coat of the eye, or **choroid** as it is called, is vascular, pigmented and elastic, and corresponds with the pia mater of the brain, and between it and the sclerotic is a system of lymph spaces corresponding with the arachnoid. The choroid is the thinnest of the three coats of the eyeball, but as it is followed forwards to the region of the corneo-sclerotic junction it increases greatly in thickness and is largely composed of white fibrous tissue, while the inner surface is thrown into a

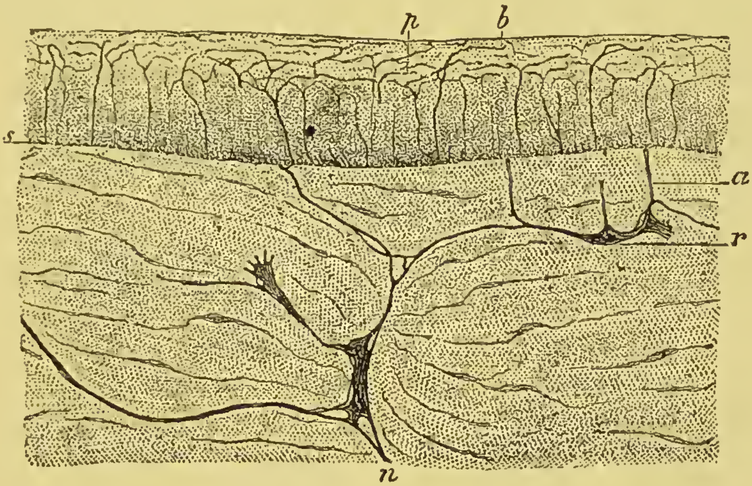

Fig. 306.—Vertical Section of Rabbit's Cornea.

n, *r*, Parts of fundamental plexus ; *a*, vertical branch passing through subepithelial plexus, *s* ; *p*, *b*, interepithelial ramifications.

series of radiating plates — the *ciliary processes.* From the corneo-sclerotic junction (Fig. 307) the middle coat is continued forward as the *iris*, separated from the cornea, however, and thus inclining towards the more central part of the globe. But the iris does not complete the choroidal investment in front, as the cornea does the sclerotic, being deficient in the region of the pupil, and thus we have a perforated screen between the light in front and the cavity of the eyeball behind. At the corneo-sclerotic junction we have the *ciliary muscle*, passing backwards to be inserted into the anterior margin of the choroid proper. In the iris are found the *sphincter* and *dilator pupilla* muscles, both of which, like the ciliary muscle, are composed of non-striped fibres.

The choroid proper—the vascular coat of the eye—consists largely of elastic fibres and pigmented connective tissue cells imbedded in a homogeneous matrix. Blood-vessels and perivascular lymphatics are found in it, and lymph spaces are abundant. It may be described in three layers. Of these, the outermost is separated from the sclerotic by the perichoroidal lymph space, and is composed of thin homogeneous lamellæ, pervaded by networks of elastic fibres and containing pigment cells. It is known as the *lamina supra choroidea.* The middle layer, or choroid proper, containing the large arteries and veins, possesses a homogeneous matrix supporting elastic fibres and pigment cells. The inner part of this layer, containing the capillaries into which the larger vessels break up, is termed the *chorio-capillary coat.* Lining the inner surface of the choroid is a homogeneous membrane, the *membrane of Bruch*, which separates it from the retina.

Except at two points, the choroid is readily separable from the sclerotic, owing to the presence of the perichoroidal lymph space, but in the ciliary region and around the entrance of the optic nerve at the back of the eyeball they are closely adherent. In the latter situation, where the sclerotic becomes continuous with the dura mater, and the choroid with the pia, bundles of tissue from each pass through the neck of the optic nerve, constituting the *lamina cribrosa.* The *ciliary processes* and the thickened continuation of the choroid from which they project do not exhibit the differentiation into three layers noticeable in the choroid itself, and the supporting tissue is mainly of the white fibrous variety. The membrane of Bruch is continued over them, together with a layer of cubical pigmented cells, continuous with the pigmentary layer of the retina; and this in its turn is covered by a layer of clear columnar nucleated cells—the *pars ciliaris retinæ*—continuous with the retina proper at the line of the *ora serrata*, which marks its anterior margin. The free extremities of many of these epithelial cells are drawn out into fine processes, with which the fibres of the suspensory ligament of the lens are continuous. In connection with the ciliary enlargement must be noted the ciliary muscles, the spaces of Fontana, and the pectinate ligament, which are described below. The *iris* is covered anteriorly by a layer of flattened epithelial cells, continuous with those lining the back of the cornea and the rest of the anterior chamber of the eye; while the body of the iris itself is composed of ordinary connective tissue supporting large blood-vessels, except in its anterior part. Pigment cells are numerous in the connective tissue, especially in deeply coloured eyes. The membrane of Bruch thins away upon the posterior

surface of the iris, and behind it is found a layer of cubical pigment cells continuous with those covering the ciliary processes, and therefore representing the pigmentary layer of the retina. The pigmentary layer of the retina and its continuation over the ciliary processes and the back of the iris represent the outer wall of the original optic cup; the sclerotic, choroid, and body of the ciliary processes and iris being derived from the mesoblast.

Behind this pigmented layer is another, also pigmented, and not consisting of clear cells, as we might expect, for it is the continuation forwards of the pars ciliaris retinæ. The two layers of pigment cells are not distinct from each other in vertical section, in which they appear as a dark band with a somewhat irregular contour, which is sometimes called the *uvea*,

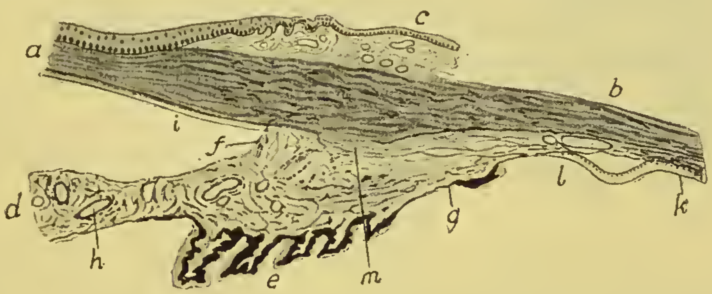

Fig. 307.—Section of Eye of Ox (Corneo-sclerotic Junction).

a, Cornea; *b*, sclerotic; *c*, conjunctiva; *d*, iris; *e*, ciliary processes; *f*, ligamentum pectinatum iridis; *g*, pars ciliaris retinæ; *h*, blood-vessels; *k*, retina; *l*, ora serrata.

and terminates abruptly at the edge of the pupil. The retina proper, the pars ciliaris retina, and the posterior layer of the uvea represent the inner wall of the original optic cup; the vitreous humour and the suspensory ligament of the lens being derived from the mesoblast, while the lens itself is of epiblastic origin.

The iris contains fibres of non-striped muscle surrounding the pupil, and these constitute the *sphincter pupillæ;* others running radially and close to the posterior surface constitute the *dilator pupillæ.*

The junction of the cornea, sclerotic, and iris.—If the iris be followed outwards from the pupil, it will be found to be continued in the form of finger-like processes into the point of junction of the cornea and sclerotic; and these processes constitute collectively the *pectinate* (or comb-like) *ligament.* These finger-like processes

of white fibrous tissue pass into the connective tissue of the sclerotic, and there become lost as separate structures. The *ligamentum pectinatum iridis* forms with the cornea the *iridic angle* bounding the anterior chamber of the eye externally. The clefts between the teeth of the comb open into a series of lymph spaces lying external to the ligament, in the ciliary enlargement itself—the *spaces of Fontana.* Anterior or external to them, and in the peripheral part of the cornea, is found a large lymph space, the *canal of Schlemm*, connected both with the spaces of Fontana and the branches of the anterior ciliary veins. Thus through the clefts between the divisions of the pectinate ligament and the spaces of Fontana the aqueous humour of the anterior chamber is in communication with the venous system and the lymphatics of the ciliary enlargement and the choroid coat.

Fig. 308.—Section of Corneo-sclerotic Junction of Eye of Ox, showing disposition of Bundles of Ligamentum Pectinatum Iridis, as seen from the anterior chamber of the eye.

A, Cornea; B, ligamentum pectinatum iridis, iris, and ciliary processes; *a*, anterior epithelium of cornea; *b*, fibrous laminæ of cornea; *c*, posterior elastic lamina pierced by bundles of ligamentum pectinatum iridis, *d*; *f*, sections of blood-vessels in iris; *g*, connective tissue of ciliary process; *h*, epithelium of ciliary process; *e*, pigment layer of ciliary process; *d'*, lymph space between bundles of ligamentum pectinatum iridis, lined with squamous epithelium.

The *ciliary muscle*, which is of special importance in connection with "accommodation," is attached to the inner surface of the corneo-sclerotic junction, immediately external or posterior to the point of entrance of the strands of the pectinate ligament, from which point it passes radially backwards to be inserted into the anterior part of the choroid. It is a somewhat fan-shaped muscle in section, the apex of the fan corresponding with its origin, and the base with its insertion.

The **optic nerve** and **retina** are developed from a hollow outgrowth from the first cerebral vesicle, which becomes invaginated to form the optic cup. The innermost of the three coats of the eye—the retina—is thus essentially nervous in origin. The optic nerve pierces the sclerotic, choroid and pigmentary layer of the retina and immediately expands into the retina proper, which forms the posterior three-fourths of the inner retinal cup and terminates

at the ora serrata, a little behind the ciliary processes. As the optic nerve pierces the sclerotic and choroid its nerve-fibres lose their medullary sheath and pass into the eye as axis-cylinders alone; and thus the nerve is constricted at the point where the loss occurs, so that a neck is formed (Fig. 309).

When the nerve has passed the level of the outer retinal cup its fibres spread out in every direction to line the inner surface of the eyeball as far as the ora serrata. At the point of divergence of the fibres a central depression, surrounded by a raised ring, occurs, which is termed the "optic disc." This is necessarily insensitive to light, as no part of the retina can be behind it,

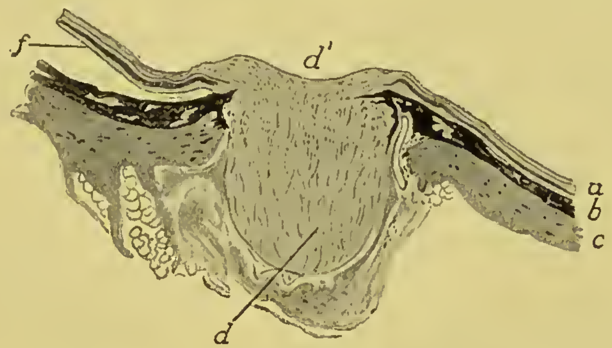

Fig. 309.—Section of Eye of Rabbit showing entrance of Optic Nerve.

a, Retina; *b*, choroid; *c*, sclerotic; *d*, optic nerve; *d'*, optic disc; *f*, layer of rods and cones.

and constitutes the "blind spot." The fibres of the optic nerve lining the eyeball form the innermost layer of the retina, the rest of which lies between these and the layer of pigment cells on the inside of the membrane of Bruch—the pigmentary layer representing the retinal portion of the outer wall of the original optic cup. "With the exception of the pigmentary layer, the nerve-fibres are continuous with all the layers of the retina. On this account, and also because of the separate origin of the pigment cells from the outer wall of the optic cup, it is sometimes convenient to speak of the 'retina proper' as indicating the portion in direct relation with the nervous system, *i.e.*, all the layers except the pigmentary one. But, speaking in a more general way, without the intention of drawing a distinction between the nervous and pigmentary layers, the term 'retina' may be considered to include both." The layers of the retina are described on page 580.

The **lens, vitreous humour, and suspensory ligament.**—The lens is retained in position behind the iris by the suspensory ligament, through which it is connected with the ciliary processes and the ciliary enlargement generally. The vitreous humour fills the main cavity of the eyeball behind the lens, and, like the suspensory ligament, is developed from mesoblast entering the eye through the choroidal fissure.

The *lens* is transparent and elastic and is enclosed in a readily separable cuticular capsule. It is composed of a number of "lens fibres," which are elongated, hexagonal prisms with serrated edges interlocking with those of their neighbours. These fibres result from the elongation of the posterior cells of the epithelial invagination from which the lens is developed. It commences as an involution of the epiblastic epithelium, which becomes separated from the surface and sinks as a closed sac within the orifice of the retinal cup. The cells of the posterior sac wall lengthen, thus filling the cavity and abutting against the anterior layer of nucleated cubical cells, which persist in this form throughout life, constituting the "anterior epithelium" of the developed lens. The transition between the anterior and the posterior cells can readily be seen in sections taken through the lens in an early period of development. In the adult lens the fibres are arranged in concentric layers, somewhat like the coats of an onion, and there are other special features of their disposition.

The *vitreous humour* is developed from mesoblastic tissue entering the optic cup with the lens, and which also becomes included in the folded stalk of the optic nerve to form the arteria centralis retinæ. It is composed of an almost structureless jelly-like matrix supporting a few branched cells, somewhat similar to those found in mucous tissue. It is invested by a distinct "hyaloid membrane," and contains, moreover, a number of somewhat similar but more delicate membranes concentrically arranged in its substance. The vitreous humour is readily separable from the retina except in the region of the optic disc, which marks the position where the retinal vessels enter it in fœtal life; and though these disappear in the course of development, yet in the adult vitreous a passage—the "canalis hyaloideus"—may be observed stretching from the disc to the lens, which at an earlier period held the retinal branches.

The vitreous humour is in contact with the inner surface of the retina, the ciliary part of the retina, the suspensory ligament and the lens.

The *suspensory ligament* (forming the "zonule of Zinn") is of considerable importance in accommodation of the eye for near and

distant objects. It secures the lens in position, and by its alternate tension and relaxation, brought about through the ciliary muscle, affects the curvature of its anterior surface. It consists of a sheet of fibrillar tissue of the white fibrous variety, the inner margin of the sheet being split into two divisions, of which the anterior becomes lost on the anterior surface, and the posterior on the posterior surface of the lens, both divisions becoming adherent to the capsule. The peripheral margin also splits, the fibres of the chief division becoming one with the processes into which the epithelial cells covering the ciliary enlargement and processes are drawn out, as already described; while the posterior division appears to pass backwards and become lost on the surface of the hyaloid membrane of the vitreous humour.

The **blood-vessels and lymphatics of the eye.**—The sclerotic, choroid and iris are supplied by the short and long posterior ciliary arteries and the anterior ciliary arteries; the retina (inner layers) by the arteria centralis retinæ. The blood from these parts is returned by the four posterior ciliary veins receiving the blood of the venæ vorticosæ, the anterior ciliary veins and the vena centralis retinæ. The rootlets of the anterior ciliary veins are in close relation to the canal of Schlemm.

The short posterior ciliary arteries pierce the sclerotic at the back of the eyeball and supply the choroid, terminating in the chorio-capillary layer. The long posterior ciliary arteries, also piercing the posterior half of the eyeball, supply the ciliary processes and iris, which are also supplied by branches of the anterior ciliary arteries, which enter the eyeball anteriorly near the insertion of the recti. The arteria centralis retinæ passes along the centre of the optic nerve to its distribution in the retina, breaking up into a capillary network in its inner layers. The outer layers of the retina are supplied indirectly through this source and the chorio-capillary layer. As a rule, the corresponding veins accompany the arteries, except the four posterior ciliary veins, receiving the blood of the venæ vorticosæ from the long and short posterior ciliary arteries, which leave the eyeball by piercing the sclerotic about its equator.

The *chambers of the eye.*—The anterior chamber is bounded by the cornea, lens and iris, and contains aqueous humour. The posterior or second chamber lies between the iris, the suspensory ligament and the ciliary processes, and communicates with the first between the iris and lens. The third chamber contains the vitreous humour, through which lymph can percolate as through a sponge. The aqueous humour is a clear watery fluid, secreted probably by the ciliary epithelium and certain glands

in the ciliary processes derived by involutions of it and the epithelium covering the posterior surface of the iris. It passes from the posterior into the anterior chamber, between the lens and the iris, thence through the clefts in the pectinate ligament to the spaces of Fontana and the canal of Schlemm, and thus into relation with the venous radicles in this region. It also passes partly into the lymph-spaces of the iris, and thus to the perichoroidal lymph-space. The fluid percolating through the vitreous humour can reach the anterior and posterior chambers through the suspensory ligament; posteriorly the cavity of the eyeball is in communication with the lymphatics of the optic nerve in the region of the optic disc.

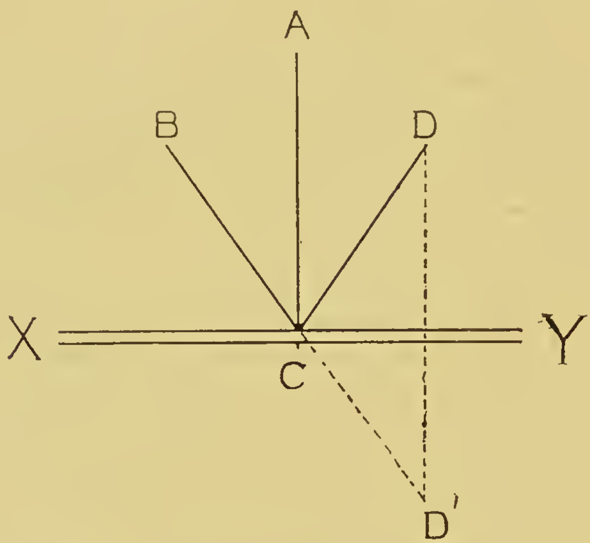

Fig. 310.—Reflection from Plane Surface.

The lymph-spaces of the sclerotic and cornea form one system, which is in communication externally with the "Tenonian cavity," and internally with the perichoroidal space. The Tenonian cavity, *i.e.*, the space between Tenon's capsule and the sclerotic, is brought, however, into direct communication with the perichoroidal space, around the paths of exit of the four posterior ciliary veins. Tenon's cavity opens into the lymph-space around the dural sheath of the optic nerve.

The retinal lymphatics are naturally in continuity with those of the optic nerve, which open into the space between the dural and pial sheaths and thus communicate with the arachnoid space of the brain.

Reflection and Refraction of Rays.

A ray of light is a series of vibrations in the ether, radiating from a luminous point in a straight line. That is to say, it travels in a straight line as long as the medium through which it passes is homogeneous. If, however, it passes from one medium into another, say from air into water, a part of the ray is *reflected*, and the remainder (the greater part) passes on through the water, but is *refracted* at the surface separating the media. But if the second medium is not transparent, but opaque (*e.g.*, polished metal), nearly all the ray is reflected.

Reflection (Fig. 310).—Let the ray of light from D fall on the surface XY at C, making an angle, DCA, with the perpendicular to the reflecting surface XY. Then the reflected ray CB will make with the perpendicular (or "normal") to the surface AC an equal angle ACB; and the eye at B will see the reflection of D as if it were at D′, the point where BC, if prolonged, cuts the perpendicular dropped from D. That is to say, *the reflected ray makes with the perpendicular the same angle as the incident ray.* And from this it follows that if the incident ray is itself perpendicular, the reflected ray follows the same path.

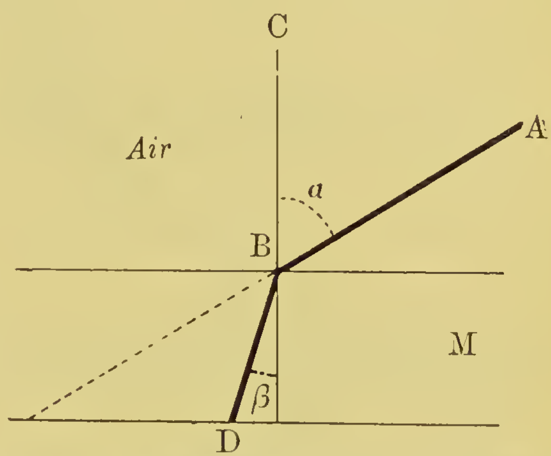

Fig. 311.—Refraction of Ray at a Plane Surface.

AB, Incident ray; BD, refracted ray; CB, the normal to the surface. When the ray passes from air into another medium, M, the refractive index of the latter is $\frac{\sin \alpha}{\sin \beta}$.

Refraction.—We may now follow the course of a ray of light passing from one medium into a second transparent one. If the ray strikes the surface, separating the two media at right angles, it passes through the second without refraction. If it strikes it otherwise, then if the second medium be denser than the first, the ray is bent towards the perpendicular; if it be less dense it is bent away from it. Let the incident ray AB pass through air and strike the surface of the second medium, M, which is water. In passing through M it is bent towards the perpendicular or normal, CB,

as the refracted ray BD. The *angle of incidence* is the angle between the normal to the surface and the incident ray; the *angle of refraction* that *between* the normal in the second medium and

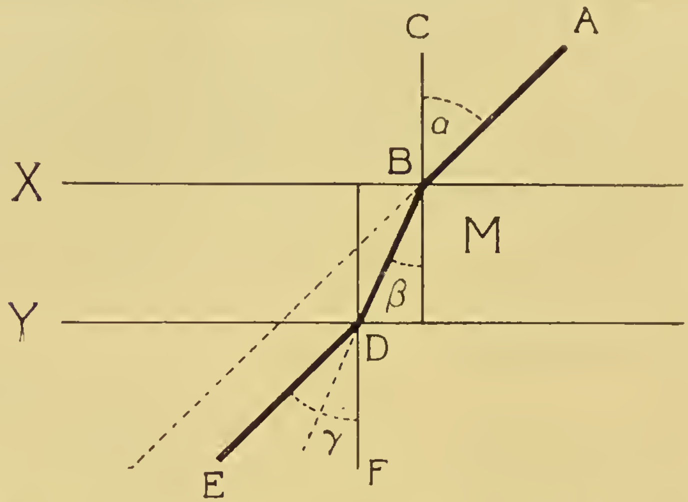

Fig. 312.—Refraction by Medium bounded by Parallel Plane Surfaces.

α, Angle of incidence; β, γ, angles of refraction.

the refracted ray. *The sine of the angle of incidence has a constant ratio to the sine of the angle of refraction*, that is for any given pair of media. This ratio, or "index of refraction," as it is called, may be expressed thus for the substance M in the figure $\frac{\sin\ \alpha}{\sin\ \beta}$.

From what has been already said, it will be apparent that when a ray passes through a medium bounded by parallel plane surfaces, it issues parallel to itself, for inasmuch as it is bent towards the perpendicular in passing from air into water, it is bent to a corresponding degree from it in passing from water into air again (Fig. 312).

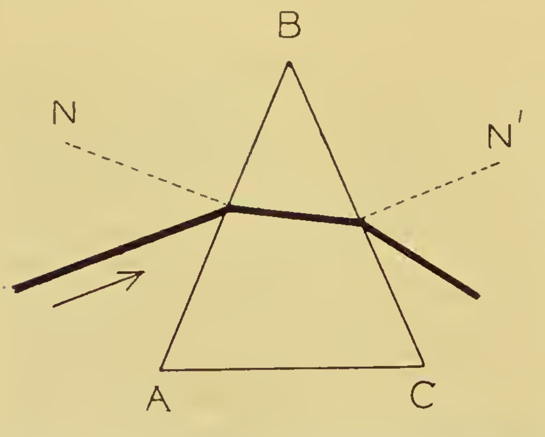

Fig. 313.—Refraction of Ray by a Prism.
N, Normal to incident; N′, normal to refracted ray.

Refraction by a Prism.—When a beam of light crosses a prism it is bent towards the normal at the first surface, and away from the normal at the second. At either surface it is bent towards the base of the prism. Thus in Fig. 313 the ray of light crossing AB is bent towards the normal N, and on crossing BC, away from the normal N′. In both cases it is inclined towards the base of the prism, AC.

Refraction by a Biconvex lens.—The centre of each spherical surface is *the centre of curvature.* The line joining the two centres of curvature is called the *chief* or *principal axis* (Fig. 314, *aa′*), the centre of the line being the *optical centre* of the lens, O. Rays passing through the optical centre do not suffer refraction, but pass unbent. Any straight line other than the principal axis passing through the optical centre is a *secondary axis* (*bb′*).

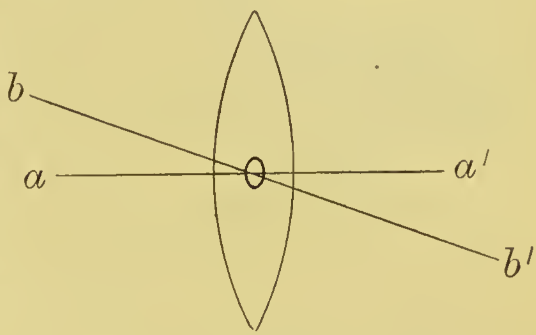

Fig. 314.

O, Optical centre of a converging (biconvex) lens; *aa′*, chief axis passing through the centre of both spherical surfaces; *bb′*, secondary axis.

Rays parallel to the principal axis are *collected* or *focussed* on the other side of the lens at a point in the axis called the *principal focus* (Fig. 315, *f*), and, conversely, rays proceeding from the principal focus pass out on the other side parallel with the principal axis, and hence do not meet.

Rays of light proceeding from a point in the principal axis beyond the focal point *f* are collected at, or converge to, a point in that axis on the other side of the lens. If the distance from the luminous point to the optical centre of the lens is twice the focal distance, the focus or point of convergence on the other side of the lens is twice the focal distance also. If the distance between the luminous point and the lens is more than twice the focal distance, then the point of convergence is proportionately nearer on the other side of the lens; while if the luminous point is less than twice the focal distance from the lens, the point of convergence on the other side is proportionately further away, *i.e.*, more than twice the focal distance.

Convergent rays are focussed on the other side of the lens within the principal focus, and, conversely, divergent rays pro-

ceeding from a luminous point within the focal distance pass out on the other side divergent (Fig. 315, B).

The same laws obtain if the luminous point is placed in a secondary axis, or in the case of rays parallel to a secondary axis, but the angle between the secondary and principal axis must be small if the focus is to be sharp.

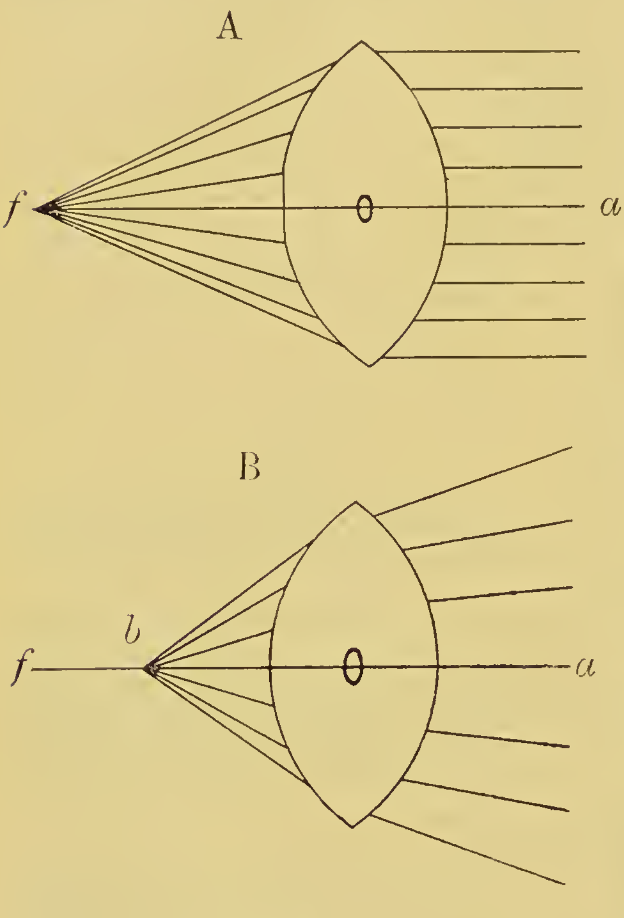

Fig. 315.

A, Parallel rays (a) are focussed or collected at the principal focus (f), and, conversely, rays proceeding from the luminous point (f) pass out at the other side parallel. B, Convergent rays (a) are focussed at a point (b) within the principal focus, and, conversely, rays proceeding from the luminous poiut (b) within the principal focus pass out on the other side divergent. O, Optical centre of lens; f, a, principal axis.

Formation of Images by Biconvex Lenses.—The image formed by a convex lens may easily be constructed from what we already know of the action of convex lenses, by projecting images of different points in the object. Let la be the object, then of the rays proceeding from the point l, lv will pass through the optical centre of the lens and will not be refracted, but all other rays from the same point will be refracted and focussed at the point v in the secondary axis lv. Thus, the image of l will be projected at v. Similarly, the image of a will be projected at b, and thus the image of la as a whole is projected in the line bv, for all the intermediate luminous points between l and a are focussed at corresponding points in bv: the image bv is

real and *inverted.* A biconvex lens can only form this inverted image if the object is beyond the principal focal point, for rays

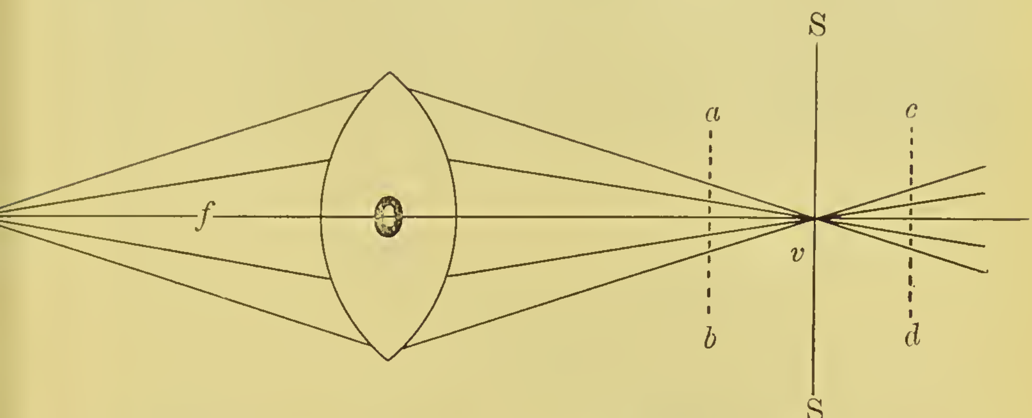

Fig. 316.—Diagram illustrating action of Biconvex Lens in Rays of Light.

Rays from *l* at twice the focal distance *f* are focussed at *v*, the same distance. As *l* approaches or recedes from the lens, *v* recedes from or approaches it. O, Optical centre of lens.

from luminous points at the focal distance or within it are not collected or focussed on the other side. Similarly, from what we have seen, if the object is at twice the focal distance from the

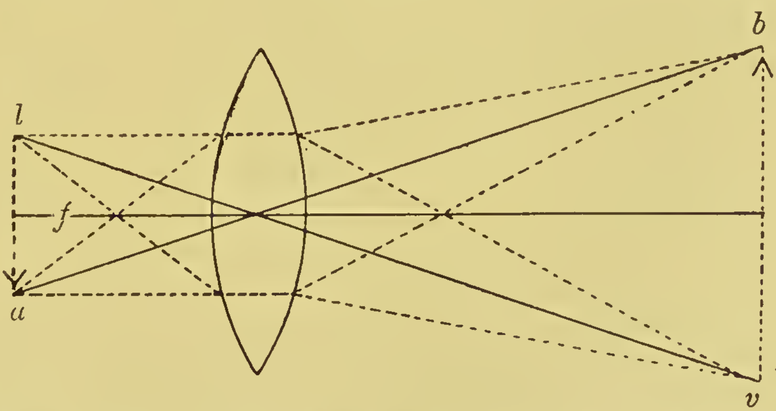

Fig. 317.—Diagram to show Formation of Image by a Convex Lens.

b, Focal point of object *a*; *v*, focal point of object *l*; thus *la* is inverted on screen; *f*, focal point of lens.

lens, its image will be the same size and at the same distance from the lens. If the object is at more than the focal distance, but less than twice that distance, the image is larger than the

object itself, and projected at a point more than twice the focal distance on the other side. If the object is at a greater distance from the lens than twice the focal distance, the image is projected at a point within twice the focal distance on the other side, and is smaller than the object itself. If the latter is so far distant that the rays proceeding from it are virtually parallel, the image is projected at the focal distance itself.

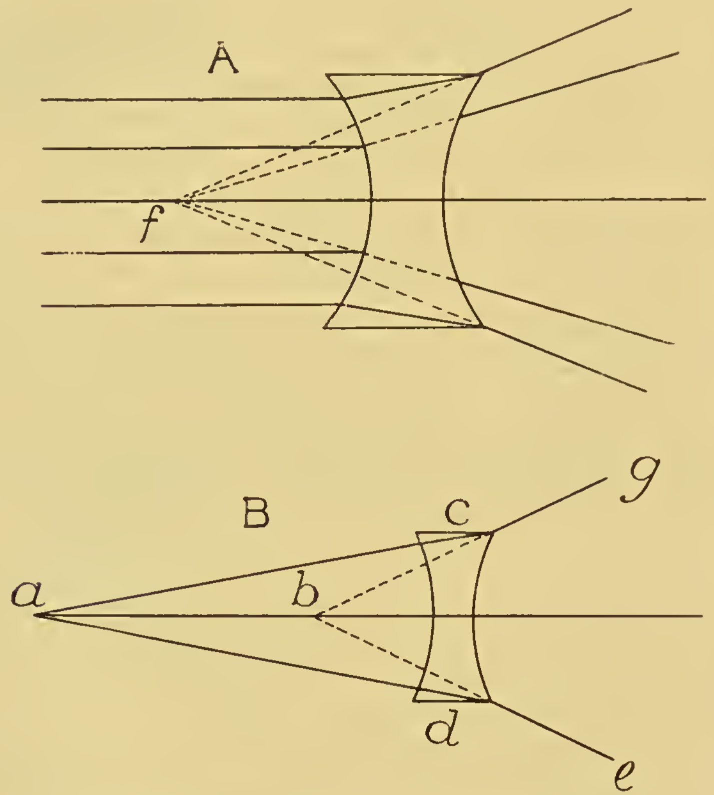

Fig. 318.—Refraction by a Biconcave Lens.

A, Refraction of parallel rays; B, refraction of divergent rays; *f*, *b*, points of focus.

Refraction by a Biconcave Lens.—Parallel rays (Fig. 318, A) are made divergent, and hence are not brought to a focus on the other side of the lens. But if the diverging rays are prolonged backwards they are collected in the focus *f*, from which they appear to be derived. Divergent rays (Fig. 318, B) may also be rendered more divergent by a biconcave lens, and if the refracted rays be prolonged backwards they meet, as before, at a focus, *b*, from which they appear to proceed.

Formation of Image by Biconcave Lens.—The image formed by a biconcave lens may be constructed in much the same way as that formed by a biconvex one. If XY is the object, then a pencil of rays proceeding from X will be rendered more divergent in passing through the lens L. If the divergent lines be prolonged backwards they will meet at a focus x in the secondary axis XG. Similarly, the pencil of rays from Y will be focussed at y. The image is virtual (*i.e.*, does not really exist in space) and erect, not inverted.

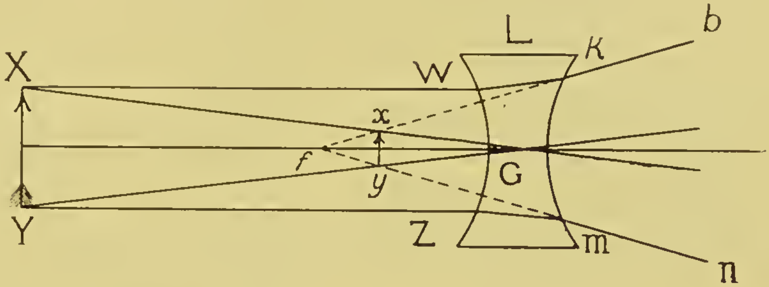

Fig. 319.—Formation of Image by Biconcave Lens.

Refraction in the Eye—Listing's "Reduced Eye."—The degree to which a ray of light is bent or refracted when it passes through a curved surface is determined by the radius of the curvature of the surface and the difference between the refractive indices of the media concerned. The greater the curvature, or in other words the smaller the radius of curvature, and the greater the difference in the refractive indices, the greater is the refraction of the ray. The study of refraction in the eye and the formation of the retinal image is complicated by the fact that the rays of light have to pass through several media with different refractive indices, and, moreover, these media are separated by surfaces of different curvature. Thus, the anterior surface of the cornea and the anterior and posterior surfaces of the lens all act as refracting surfaces, while the cornea, the aqueous and vitreous humours, and the lens possess different refractive indices. The following figures may be noted, and it will be observed that some of the radii of curvature, and consequently the distances also, vary for near and far vision.

Refractive Indices:

Air, ...	1·000
Water, aqueous humour, vitreous humour and cornea, . .	1·336
Lens (mean of all layers), . .	1·437

Radius of Curvature:

	Far Vision.	Near Vision.
Cornea,	7·8 mm.	7·8 mm.
Anterior surface of lens,	10·0 "	6·0 "
Posterior surface of lens,	6·0 "	5·5 "

Distance between:

Anterior surface of cornea and anterior surface of lens,	3·6 mm.	3·2 mm.
Anterior surface of cornea and posterior surface of lens,	7·2 "	7·2 "
Anterior and posterior surface of lens,	3·6 "	4·0 "
Posterior surface of lens and retina,	15·0 "	15·0 "
Antero-posterior diameter of eye along the axis,	21·8 "	21·8 "

But from these data it is possible to reduce the different refractive indices to one mean, and the different refracting surfaces to one curved surface of known curvature. When this is done, and a schematic or "reduced" eye thus constituted, we have the following figures:—

Radius of curvature of single refracting surface	5·12 mm.
Index of refraction of single refracting medium	1·35 "
Distance of refracting surface from principal focus	20·00 "
Distance of refracting surface behind anterior surface of cornea	1·8 "
Distance of nodal point (the point through which rays pass without refraction) of reduced eye from its anterior surface	5·0 "
Distance of nodal point from the principal focus	15·0 "

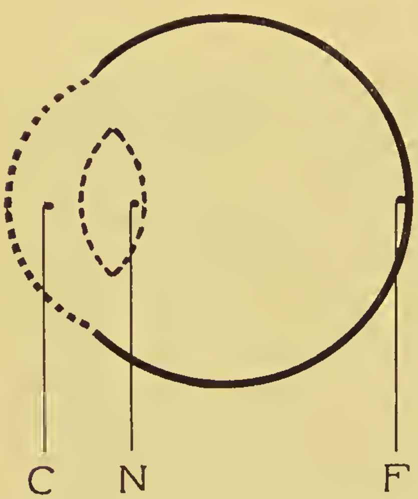

Fig. 320.—Diagram of Reduced Eye.

C, Single refracting surface 1·8 mm. behind anterior surface of cornea; N, nodal point; F, principal focus.

The nodal point is the centre of the circle of which the single refracting surface is part. Rays passing through the nodal point are not refracted. The nodal point of the reduced eye is situated towards the posterior surface of the lens. The single refracting surface is situated about midway between the posterior surface of the cornea and the anterior surface of the lens. The retina would lie in the principal focus, *i.e.*, 15 mm. behind the nodal point.

Formation of the retinal image.—The image of an object formed on the retina in distinct vision is real and inverted. Let AB be the object. Then the rays passing from the luminous point A will be focussed at the other side of the lens at *a*, in the line of the ray of direction A*a*, which passes through the nodal point N and is not itself refracted. Similarly, a pencil of rays from B will be focussed at the point *b* in the ray of direction B*b*, which, passing through the nodal point, is not itself refracted, for, like the ray A*a*, it cuts the refracting surface at a right angle. Thus, the position of the image on the retina may be obtained by drawing straight lines from the periphery of the object through the nodal point, prolonging them till they cut the retina, and inasmuch as the lines necessarily cross in the nodal point, the image is inverted.

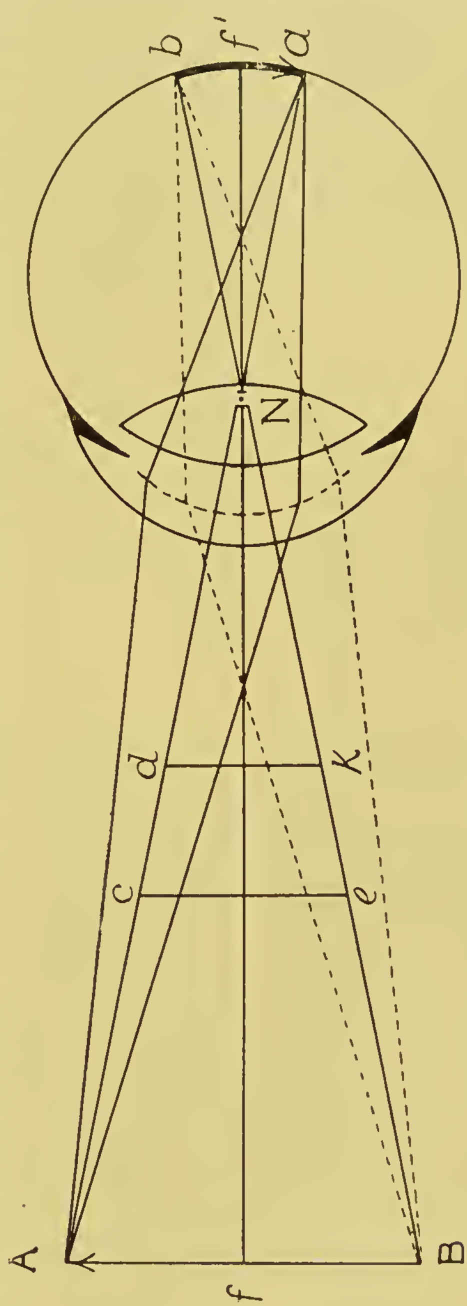

Fig. 321.—Diagram Illustrating the Formation of the Retinal Image.

The angle between the lines joining the periphery of the object and the nodal point is termed the *visual angle*, and is of course equal to the other angle formed by the prolongation of the lines towards the retina. If the distance of the object from the eye is constant, the visual angle will vary with its size; if the object be the same, the visual angle will vary inversely as the distance. The size of the retinal image may readily be calculated if the distance of the object and its size be

known, for the triangles of which ab and $a'b'$ are the bases, and the nodal point the apex, are similar triangles. Let the distance from a to the nodal point be represented by x, and from the nodal point to a' by y. Then $\frac{ab}{x} = \frac{a'b'}{y}$, and of these quantities only $a'b'$ is unknown. Thus if the object be 4 inches in size and 10 feet (120 inches) away, then $\frac{4}{120} = \frac{a'b'}{15}$ (the distance in mm. of the nodal point from the retina) and $a'b' = \frac{4}{120} \times 15 = \frac{60}{120} = \frac{1}{2}$ mm.

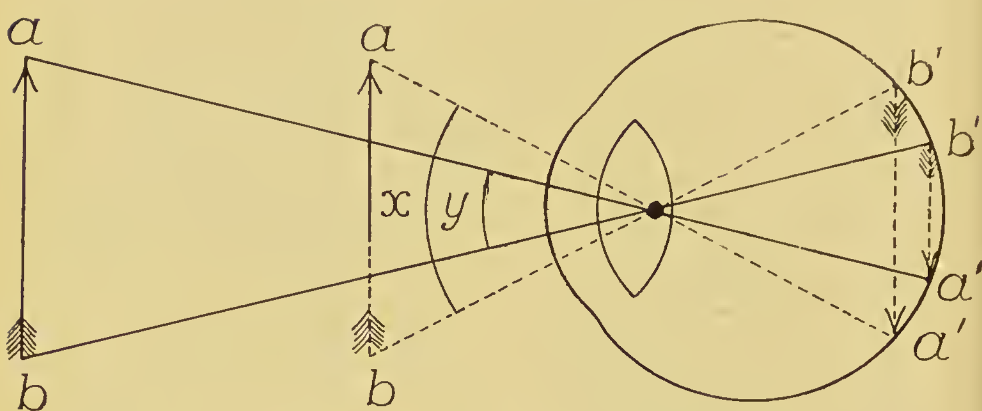

Fig. 322.—Diagram of Relation between Visual Angle and Retinal Image.

x, Visual angle when ab is near; y, when it is distant.

Accommodation.—By accommodation is meant the change taking place in the visual apparatus whereby either far or near objects are focussed upon the retina. If an object, lens, and screen be so arranged that the object is brought to a distinct focus upon the screen, it is found that on decreasing or increasing the distance between the object and the lens its image becomes blurred. This in the first case is because the rays are brought to a focus behind the screen, and in the second because they have been brought to a focus in front of it, thus crossing each other and becoming divergent ere they reach it. In each case diffusion circles are obtained and not a distinct image. This of course may be rectified by moving the screen backwards or forwards, so that its plane may again include the focal point, as is done in focussing with a photographic camera. But in man the distance between the lens and the screen (retina) is fixed, so that some other means must be found of obtaining a distinct image of an object at different distances. This is accomplished by alterations in the

curvature, and hence in the refractive power of the lens, the curvature decreasing as the object is withdrawn, and increasing as it is brought nearer to the eye. And thus, however great or small (within limits) the distance of the object from the eye may be, the rays proceeding from it are focussed sharply on the retina; though of course a near and distant object cannot be seen with equal distinctness at the same moment.

That accommodation is the result of changes in the curvature of the lens is indicated by the fact that if the lens be removed for cataract the power of accommodation is lost. That such changes in its curvature take place may, however, be much more readily demonstrated by the following experiment—the experiment known as *Purkinje-Sanson's Images.* If a lighted candle be held a little to one side of the observed eye, three reflections of the flame may be seen in it —(a) a bright, small, erect image from the anterior surface of the cornea; (b) a larger image, also erect but less bright, from the anterior surface of the lens; and (c) a smaller, indistinct, inverted image from the posterior concave (forwards) surface of the lens. During this part of the observation the observed eye has been at rest, *i.e.*, accommodated for distant objects. If now the eye be accommodated for near vision, *e.g.*, by looking at some near object, such as the finger of the observer held a few inches from the face, the second image alters in size and position, becoming smaller, somewhat brighter, and approaching the first; and the process is reversed, the second image enlarging and receding from the first, if vision be directed again towards the horizon. The first and third images remain practically unaltered throughout the experiment. This observation shows that in accommodation for near vision the cornea and posterior surface of the lens remain unaltered, while the curvature of the anterior surface of the lens is increased, bringing it nearer to the cornea. Sanson's images may also be seen with the *phakoscope* of Helmholtz. This is a triangular box blackened inside (Fig. 324). The observer's eye is at the window, K, and the observed eye opposite A. At PP′ two prisms are arranged and a lighted candle is placed in front of them. Three pairs of images

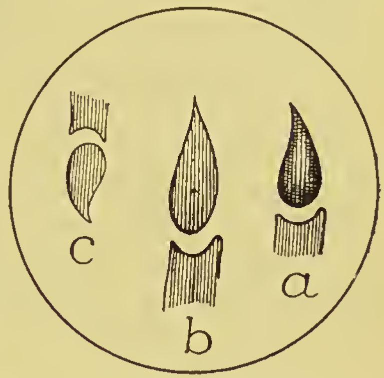

Fig. 323.—Images of Candle Flame.

a, Image reflected from anterior surface of cornea (bright, small, erect); b, from anterior surface of lens (less distinct, larger, erect); c, from posterior surface of lens (smaller, indistinct, inverted).

are now seen in the observed eye, which is at first resting, *i.e.*, accommodated for distant vision. If now the person whose eye is under observation accommodates for a near object, such as the ivory needle which may be pushed up at A, the second pair of images become smaller and approach the first pair and each other.

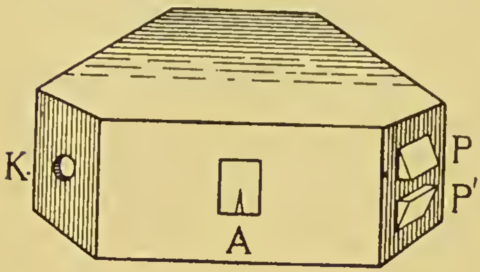

Fig. 324.—The Phakoscope.

By *negative accommodation* is meant the condition of rest, when the curvature of the lens is such that it focusses parallel rays (*i.e.*, those proceeding from distant objects) upon the retina. This is the condition of the passive normal or *emmetropic* eye. No muscular action is required, and consequently there is no feeling of effort on looking at distant objects.

Positive accommodation, on the other hand, is required if rays proceeding from a near object are to be focussed on the retina, and this involves contraction of the ciliary muscle to secure the increase in the anterior curvature of the lens.

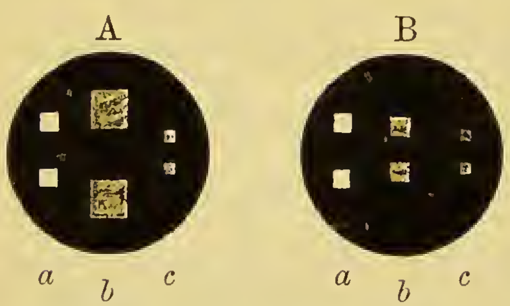

Fig. 325.—Purkinje-Sanson's Images as seen with the Phakoscope.

A, As seen in negative accommodation; B, as seen in positive accommodation.

The mechanism of accommodation appears to be, shortly, as follows* :—During rest, *i.e.*, in the condition of negative accommodation, the ciliary muscle is relaxed and the suspensory ligament tense, and by its tension the lens is maintained in a flattened condition against the anterior surface of the vitreous humour. When positive accommodation is initiated the ciliary muscle contracts and pulls forward the choroid coat, into the anterior part of which its fibres are inserted. The zonule of Zinn (suspensory ligament) is thus relaxed, and the tension on the anterior part of the capsule of the lens diminished. The latter, in virtue of its elasticity, assumes a more convex form, bulging forwards as soon as

* This is the original explanation of Helmholtz, which may still be accepted as the most generally satisfactory that has been put forward. Other explanations have been suggested, but they do not agree with all the facts of the case so well.

the tension of the zonule is removed. When the passive state of the eye is resumed the ciliary muscle relaxes, the tension of the zonule on the lens returns, and the anterior surface of the latter becoming flattened parallel rays are again focussed on the retina. During positive accommodation the contraction of the ciliary muscle and its maintenance in this condition, as in reading, produces a *sense of effort*, which disappears if the eyes be closed or allowed to fall on more distant objects. There is then no sense of effort, the accommodation being purely negative.

Near and far points of vision.—In speaking of accommodation, it was stated that by this means rays from an object, either far or near, could be focussed upon the retina. It was indicated, however, that this only held within certain limits, and this brings us to the consideration of the range of distinct vision. By the *far point* is meant the greatest distance at which an object may be seen distinctly; and as parallel rays, *i.e.*, those from a point more than 65 metres distant, are focussed in the retina when the eye is at rest, the far point lies theoretically in infinity. The distance will, however, be limited by the size of the object, the condition of the atmosphere, and the curvature of the earth. By the *near point* is meant the smallest distance to which an object may be brought and yet seen distinctly; and the range of distinct vision lies between these two points. The far point need not detain us, but the near point and the method of its determination require some notice. It has been mentioned that positive accommodation, such as that involved in reading, is accompanied by a sense of effort, and this becomes accentuated if the type be brought gradually nearer to the eye. As the rays in this way become more and more divergent, still stronger contraction of the ciliary muscle is required in order to increase the anterior curvature of the lens, and the sense of effort is appreciably increased. At last a point is reached when only by the strongest effort is the type clearly focussed, and the effort can only be maintained for a few moments, the type becoming blurred as soon as it is relaxed. The near point of vision is thus the smallest distance from the eye at which, by a special effort of accommodation, an object can be clearly seen. It is usually about five or six inches. It may be determined in the following manner:—Two holes are pierced in a piece of cardboard at a distance from each other less than the diameter of the pupil, and the cardboard is held close to the eye. On looking through the holes at a needle held at a certain distance the rays passing through them are brought to a clear focus on the retina and the image is single. If now the needle be brought sufficiently nearer to the

cardboard, accommodation can no longer overcome the divergence of the rays and bring them to a focus on the retina—

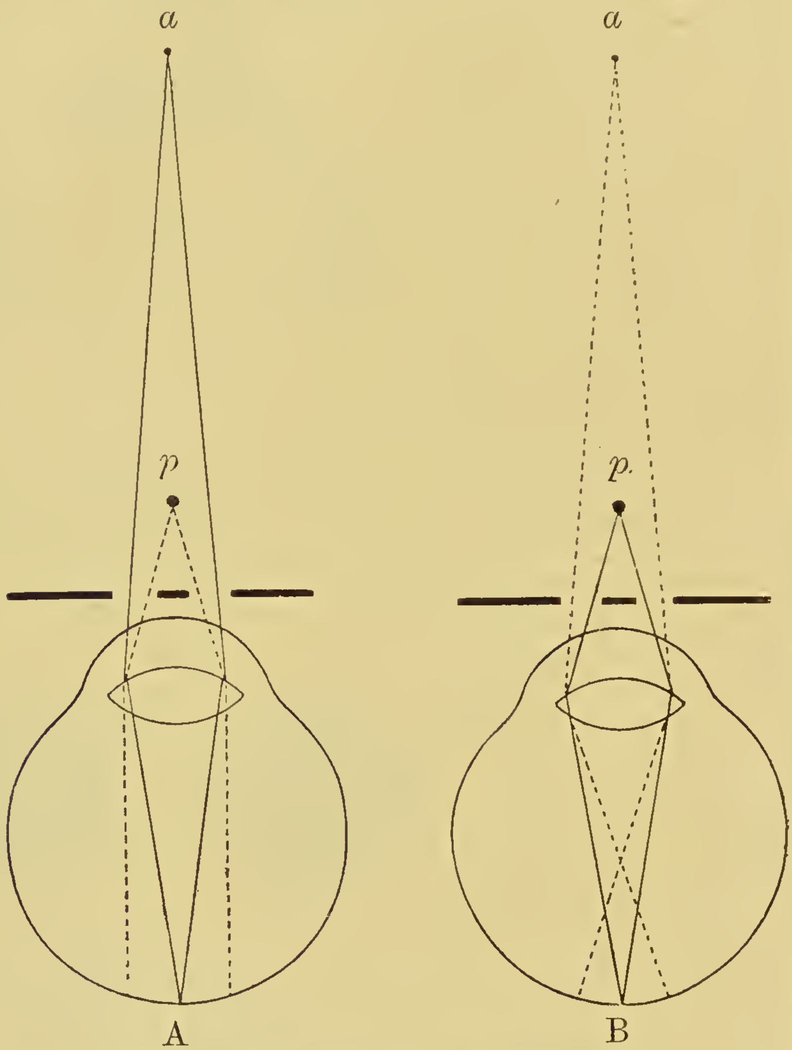

Fig. 326.—SCHEINER'S EXPERIMENT.

In B the eye is accommodated for a near object, and the needle held at *p* is focussed on the retina. If the needle is moved to *a*, the accommodation remaining the same, the rays from it are focussed in front of the retina, and crossing give a double image.

In A the eye is accommodated for a more distant object, and the needle held at *a* is focussed on the retina. If the needle be moved to *p*, the accommodation remaining the same, the rays from it are focussed behind the retina, or not at all, and again give a double image.

they are focussed behind it, or not at all, and two images are seen. If in the first part of the experiment one of the holes

be closed, the single image is still distinctly seen. If one of the holes be closed in the second part the image on the same side disappears. In this experiment (Scheiner's) the near point of vision is determined as the nearest point at which a single clear image is possible. If the eye be now accommodated for this point and the needle held at a greater distance, two images are again seen, for the rays have been focussed and have crossed in front of the retina. If one of the holes be stopped it is now the image on the opposite side which disappears.

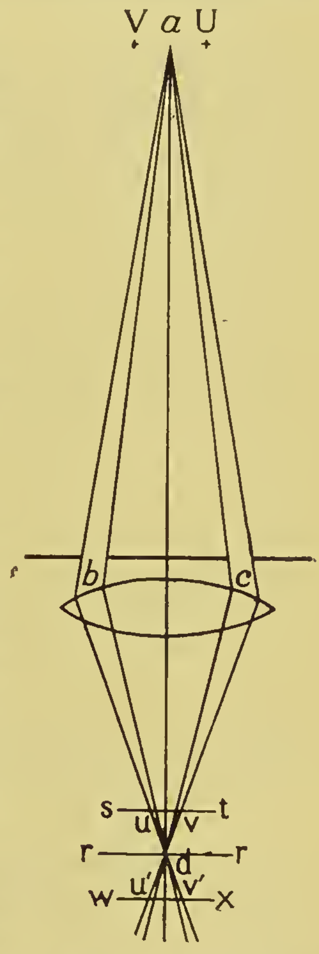

Fig. 327.—Scheiner's Experiment.

During accommodation* the eyes converge owing to the action of the internal recti muscles of the eyeball. The pupil also diminishes in size from contraction of the sphincter pupillæ, the iris thus cutting off the most peripheral divergent rays and securing a sharper image. These muscles, together with the ciliary muscle, are under the control of the third nerve.

Accommodation in man, as we have seen, is brought about by alterations in the curvature of the lens, and this is also true of other mammals and birds. But it is not universal throughout the animal kingdom. In fishes, the eye is accommodated for near objects already, and positive accommodation is required to focus *distant* rays on the retina. Here the curvature of the lens is not altered, but the lens itself is drawn nearer to the retina, so that rays are focussed upon it which otherwise meet between it and the lens. In amphibians and snakes the opposite occurs: as in man, the eye is accommodated at rest for distant objects, but objects near at hand are focussed by an increase in the distance between the lens and the retina.

Optical defects.—1. In **myopia**, or shortsightedness, the eyeball is elongated antero-posteriorly, with the result that parallel rays are focussed in front of the retina, and only divergent rays upon it. The eye at rest, in fact, is permanently adjusted for

* "Accommodation" thus used may generally be read "positive accommodation."

near objects only, and thus both the far and near points are brought nearer to the eye, and the range of distinct vision is very small. Concave glasses, by rendering parallel rays divergent, and those already divergent more so, correct the defect.

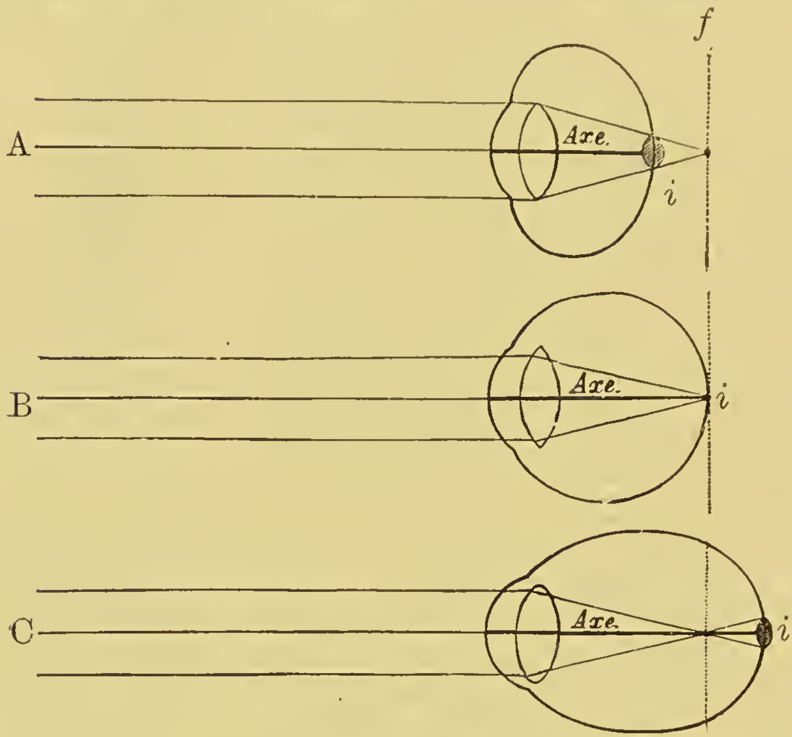

Fig. 328.—Diagrams illustrating (A) Hypermetropic Eye, (B) Emmetropic, and (C) Myopic Eye.

f, Focal point for parallel rays; *i*, image on retina; *Axe.*, antero-posterior axis of eyeball.

2. In **hypermetropia**, or longsightedness, the reverse condition is found. The antero-posterior diameter of the eyeball is less than normal, and consequently when the eye is at rest parallel rays are focussed behind the retina, and a blurred image is again the result. An effort of accommodation is required to focus distant objects, and the near point of vision is also further away than normal. Thus an object placed at the near point for the normal eye cannot by the strongest effort of accommodation be distinctly seen, as the rays proceeding from it are focussed behind the retina. Convex glasses, by increasing the refraction of the rays, remedy the condition.

3. In **presbyopia** the antero-posterior axis of the eye is normal, but through the increasing rigidity of the lens, and the weakness of the ciliary muscle which supervenes with age,

the power of accommodation for near objects is largely lost, and thus ordinary type requires to be held at an ever-increasing distance from the eye as the condition progresses. The near point of vision is therefore removed, but, unlike the hypermetropic condition, distant vision is not affected, parallel rays being still sharply focussed on the retina. Convex glasses are the remedy.

Thus, while in hypermetropia the mechanism of accommodation may be perfect and the condition is due to shortening of the antero-posterior axis of the eyeball, in presbyopia it is the mechanism of accommodation which is at fault. Atropin, which paralyses the ciliary muscle, renders the hypermetropic eye incapable of seeing distant objects, but has no such effect on the presbyopic eye. Accommodation for near objects is of course abolished in both cases.

Hypermetropia is congenital, myopia develops as the child grows up, while presbyopia usually supervenes about the age of forty-five years.

4. **Astigmatism.**—Here the cornea (sometimes the lens) exhibits usually a greater curvature in its vertical than in its horizontal meridian. The result is, that lines cutting each other at right angles, as in the case of a cross, are not brought to the same focus. When the vertical meridian of the refracting surface is the most curved, the horizontal focal line is in front, while when the horizontal meridian is the most curved the vertical focal line is in front of the horizontal. A certain measure of astigmatism is present in the normal eye, but is unnoticeable. The difference in curvature may, however, be much greater, and will then require correction, as distinct vision is impossible. The remedy lies in the use of segments of cylinders, the curvature of the segment being made to correspond with that of the meridian of least curvature in the eye.

5. **Spherical aberration.**—When a pencil of rays passes through a convex spherical refracting surface, the marginal rays are more strongly refracted than those passing more centrally, and thus are brought to a focus in front of them, so that there are many foci resulting in circles of diffusion. In the eye this difficulty is obviated (1) by the iris cutting off most of the peripheral rays, especially when the pupil contracts during accommodation for divergent rays; (2) by the fact that in the eye the refracting surfaces of the cornea and lens are not spherical but less curved towards their margins than in the centre, and thus the refracting power of the marginal

part is less than it otherwise would be; (3) by the index of refraction of the peripheral part of the lens being less than that of the central.

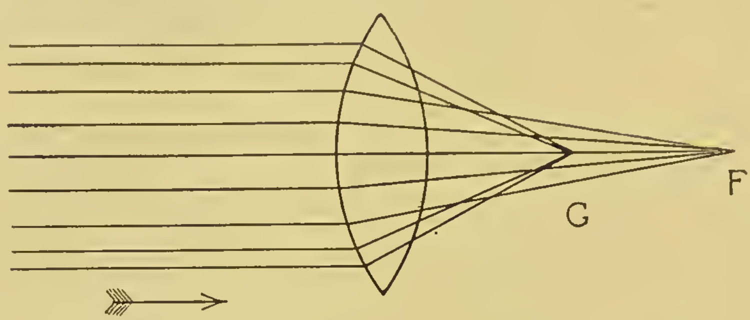

Fig. 329.—Diagram of Course of Rays in Spherical Aberration.
While central parallel rays meet at principal focus F, peripheral rays are focussed nearer the lens at G.

6. **Chromatic aberration.**—The violet rays of the spectrum are refracted most strongly, the red rays the least, and thus the violet rays are brought to a focus nearer the lens than the red. Thus, if the eye be focussed so that the red rays meet on the retina, there will be diffusion circles of the spectral colours round the focal point, with violet at the outside. If the violet rays are focussed, the contrary occurs, the red being external. But the power of dispersing the rays of white light possessed by the refracting media of the eye is so small, and the activity of accommodation so great, that this defect is of no practical consequence, though present in all eyes.

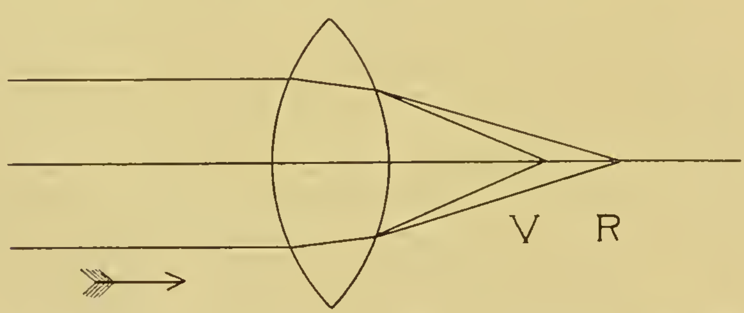

Fig. 330.—Diagram of Course of Rays in Chromatic Aberration.
V, Focus of violet rays; R, focus of red rays.

7. **Muscæ volitantes** are opaque particles, often seen floating in the field of vision during work with the microscope. They

are due to the presence of disintegrating cells, fibres, &c., in the vitreous humour. These, like the two previous defects, are found in the ordinary eye, but are of little practical significance so far as distinct vision is concerned.

Functions and innervation of the Iris.—The iris acting as a diaphragm cuts off the marginal rays and so decreases spherical aberration. Thus contraction of the pupil occurs during positive accommodation, when, on account of the divergence of the rays, spherical aberration would impair the clearness of the image. Secondly, it regulates the amount of light admitted to the eyeball, the pupil dilating in the dark and contracting in the light.

The contraction of the pupil is brought about by the *sphincter pupillæ*, the circular muscle of the iris, and dilatation by the dilator pupillæ, the radial muscle. The fibres of the sphincter are arranged immediately around the pupil, while the dilator fibres extend from the margin of the iris along its posterior surface, immediately in front of the uvea, and blend with the fibres of the sphincter internally. The size of the pupil depends on the balance between the two forces of dilatation and contraction. Some have denied the existence of special dilator fibres, and attribute dilatation of the pupil to inhibition of the circular fibres of the sphincter. But dilator fibres have for long been known to exist in the iris of the otter and birds, and it appears also that they are to be found in the eyes of rabbits, cats and

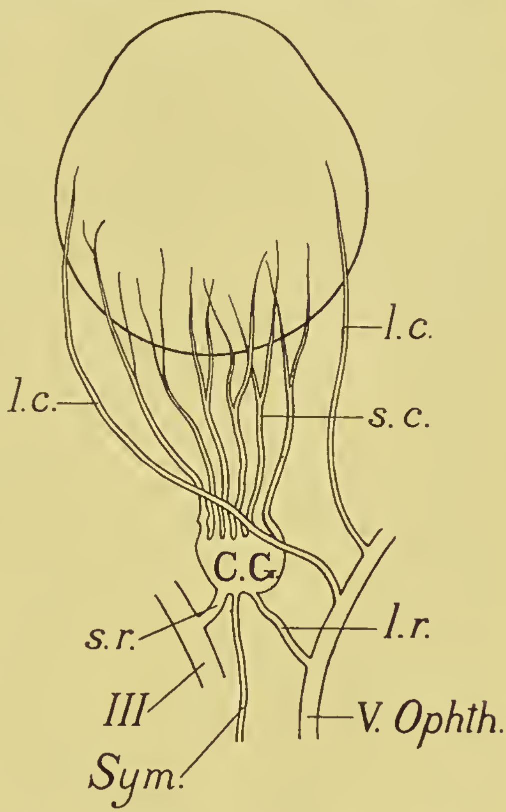

Fig. 331.—Diagram of Nerves to the Pupil.

C.G., Ciliary ganglion ; *s.r.*, its short root from the third or oculo-motor nerve *(III)*; *l.r.*, long root from nasal branch of ophthalmic division of the fifth nerve ; *s.c.*, short ciliary nerves from ciliary ganglion ; *l.c.*, long ciliary nerves from nasal branch of ophthalmic division of the fifth nerve.

dogs. Furthermore, if the iris be stimulated near its margin at different points, the pupil assumes an irregular shape, due to retraction at these points. Were the dilatation due to inhibition of the sphincter, it would be regular and not localised at the points stimulated.

The nervous supply of the iris is three-fold. The sphincter is supplied by the third or oculo-motor nerve, the dilator pupillæ by the sympathetic, while the fifth supplies sensory branches.

If the third nerve be divided, dilatation of the pupil results, and contraction may be induced by stimulating the peripheral end of the cut nerve. If the sympathetic be divided, the pupil contracts, and dilatation may be induced by stimulation of the peripheral (cephalic) end of the cut nerve (cervical sympathetic). If both nerves be stimulated together, contraction overcomes dilatation.

Both contraction and dilatation may be brought about reflexly. Thus, when the eye is subjected to a bright light, contraction of the pupil occurs, the afferent nerve being the optic and the efferent the third. The same result is obtained if the optic nerve be stimulated artificially. It is to be noted that both pupils contract when the light falls on either retina, due to the inter-central communication between the two pupilo-constricting centres in the floor of the aqueduct of Sylvius. In fact, the pupils work together on account of this inter-central communication unless the cause of contraction or dilatation of either of them is purely local—*e.g.*, if the nerves on either side be injured or drugs locally applied. The contraction of the pupil in accommodation is also reflex, but the reflex path is not the same, for in locomotor ataxia the light reflex may be absent, while the reflex for accommodation is unimpaired (Argyll Robertson symptom). Here the lesion is probably situated between the corpora quadrigemina and the oculo-motor centre. Reflex dilatation of the pupil is caused by dyspnœic blood, painful stimulation of sensory nerves, labour pains, or even by slight tactile impressions, such as tickling the palms. The starting of the eyeballs from their sockets, mentioned in accounts of the torture chamber, is due to contraction of the muscular fibres in Tenon's capsule, which are also under the control of the cervical sympathetic.

The reflex centre for dilatation lies in the medulla oblongata. The efferent fibres pass downwards and leave the cord in the anterior roots of the first, second and third dorsal nerves, passing upwards in the cervical sympathetic. The term *cilio-spinal region* is applied to the lower cervical and upper dorsal part of the cord,

from its relation to these fibres, but it must not be taken as indicating the presence of any distinct centre.

Apparently, however, there is some local mechanism in the eye itself for regulating the size of the pupil, for the excised eye of the frog exhibits constriction of the pupil in a bright light and dilatation in the dark.

Effect of drugs on the iris.—(1) *Mydriatics.*—These dilate the pupil, and include atropin, daturin, cocaine and hyoscyamin. When a solution of atropin is dropped into the eye, dilatation occurs principally from paralysis of the third nerve, but the dilator pupillæ is itself stimulated; for if dilatation be produced by division of the third nerve, the local application of atropin leads to a further increase in the size of the pupil. If atropin be dropped into one eye that pupil alone is affected, the other, if anything, becoming constricted from the reflex effect of the greater quantity of light falling on the retina of the atropinised eye. The application of the drug also causes dilatation of the pupil of the excised eye. Taken internally, atropin produces dilatation of the pupil on both sides. Applied either locally or introduced into the blood-stream it causes paralysis of the ciliary muscle, and so temporary loss of accommodation. Cocaine is also a powerful anæsthetic, and a 4% solution is commonly used for producing insensibility of the cornea. (2) The *myotics*, viz., physostigmin (eserin), muscarin, pilocarpin and morphia cause paralysis of the dilator fibres and stimulate the fibres of the third nerve, thus producing contraction of the pupil. Morphia acts when taken internally, that is to say, the action is central, not peripheral. The myotics generally cause spasm of the ciliary muscle, rendering negative accommodation impossible. The mydriatics and myotics can be played off against each other. (3) *Anæsthetics.*—In chloroform administration during the stage of excitement the pupillo-dilator centre is stimulated and the pupil expands. Afterwards, as stupor supervenes, the centre becomes paralysed and that of the pupillo-constrictor stimulated, producing constriction of the pupil. Still later this centre in its turn is paralysed and the pupil again dilates. Anæsthetics, such as chloroform, alcohol and ether, generally cause contraction of the pupil when stupor commences, going on ultimately to dilatation if the action of the drug is prolonged.

Structure of the Retina.

The optic cup, as we have seen, is composed of an inner and an outer part; the former in the developed eye consists of the

retina proper, the pars ciliaris retinæ, and its pigmented continuation over the back of the iris; the latter of the pigmentary layer of the retina and its continuation as a layer of pigmented cells over the ciliary processes and the back of the iris. The optic nerve, piercing the coats of the eyeball posteriorly, expands immediately into the retina proper, which, ceasing anteriorly at the ora serrata, corresponds with the posterior three-fourths of the optic cup. The point of entrance of the optic nerve is marked by the optic disc, a little to the inner side of the antero-posterior axis, which passes through a small depression—the *fovea centralis*—forming the centre of the *macula lutea* or *yellow spot.* The optic nerve-fibres spread over the inner surface of the retina, forming the most internal of its nervous layers, and are physiologically connected with the nerve elements of the layers between it and the hexagonal pigment cells. The following are the layers of the retina from within outwards:—(1) The internal limiting membrane, (2) the layer of nerve-fibres, (3) the layer of ganglion nerve-cells, (4) the inner molecular layer, (5) the inner nuclear layer, (6) the outer molecular layer, (7) the outer nuclear layer, (8) the outer limiting membrane, (9) the layer of rods and cones, and (10) the layer of hexagonal pigment cells. The rods and cones, together with their rod and cone nuclei and fibres in the outer nuclear layer, constitute the terminal sense cells of the eye, and are brought into relation through the rest of the retina with the nerve-fibres of the second layer.

Like other parts of the central nervous system, the retina consists of supporting or neuroglial tissue as well as the nervous elements proper, and, in addition, there is the layer of hexagonal pigment cells. We may conveniently consider its more intimate structure, therefore, under these heads—(1) neuroglial, (2) nervous, and (3) pigmentary.

1. The **neuroglial** or **supporting tissue** derived from the epithelium of the neural column is represented by the *fibres of Müller*, extending from the internal to the external limiting membrane, and affording support to the nervous elements among which they pass. They are modified, elongated, epithelial cells, which at the ora serrata shorten and pass into the cells of the pars ciliaris retinæ. The innermost end of each fibre is expanded into a kind of foot, and these expanded feet, by the apposition of their margins, give rise to the internal limiting membrane. As the fibre of Müller passes through the fibrous and ganglionic layers it becomes much narrower. In the inner molecular layer it breaks up at its edges into a close network of fibrils, which themselves constitute a great part of the layer. In the

inner nuclear layer the lateral processes form a basket-work arrangement surrounding and supporting the nuclei of the nervous elements of the layer; and in this layer is found the nucleus of the fibre itself, an oval body with its axis in that of the fibre in which it lies. In the outer molecular layer the fibres again break up at their margins into a network of fibrils, and in the outer nuclear layer a basket-work is found, in this case the meshes supporting the nuclei of the rod- and cone-fibres. The basket-work is bounded by the external limiting layer, beyond which, however, a little of it projects in the form of short processes fitting between the ends of the rods and cones. The fibres of Müller are probably composed of neurokeratin.

2. The **nervous elements** of the retina are represented by—(1) The layer of nerve-fibres and ganglion cells, (2) the cells of the inner nuclear layer, and (3) the layer of rods and cones, with their fibres and nuclei in the outer nuclear layer. These different strata are in physiological continuity with each other through the molecular layers, the processes of the cells of the nuclear and ganglionic layers breaking up in the general network of fibrils forming the molecular layers.

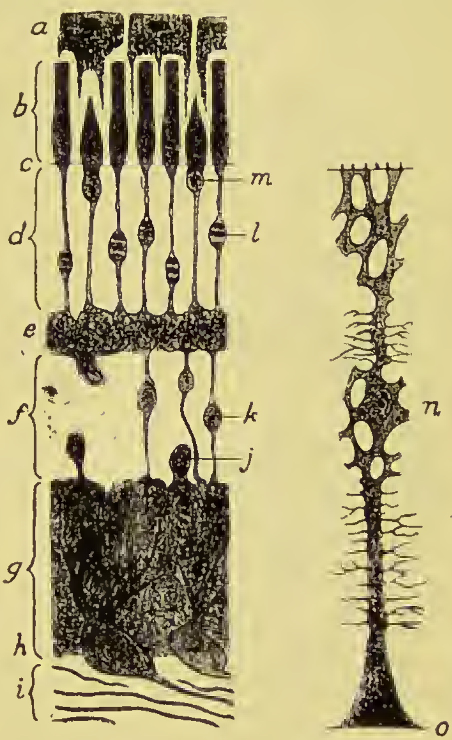

Fig. 332.—Diagrammatic representation of Structure of Retina.

a, Layer of pigment cells; *b*, layer of rods and cones; *c*, external limiting membrane; *d*, external nuclear layer; *e*, external molecular layer; *f*, internal nuclear layer; *g*, internal molecular layer; *h*, ganglion cell layer; *i*, layer of nerve-fibres; *j*, unipolar cells (spongioblasts of some authors); *k*, bipolar cells; *l*, nucleus of rod-fibre; *m*, nucleus of cone-fibre; *n*, nucleus of Müller's fibre; *o*, internal limiting membrane.

(1) *The nerve-fibre and ganglion cell layers.*—The non-medullated fibres from the optic nerve pass between the feet of the Müllerian fibres, and then turning radially outwards are either connected as axis-cylinder processes with the cells of the gan-

glion cell layer or pass directly into the inner molecular layer, in which they break up and become lost. The ganglion cells are large and somewhat globular in form, with a nucleus and nucleolus, and possess one axis-cylinder process and several peripheral ones. These pass into the inner molecular layer, where they become lost in the general network.

(2) The *inner nuclear layer* contains cells of three kinds. The greater number are bipolar, and possess a well-marked

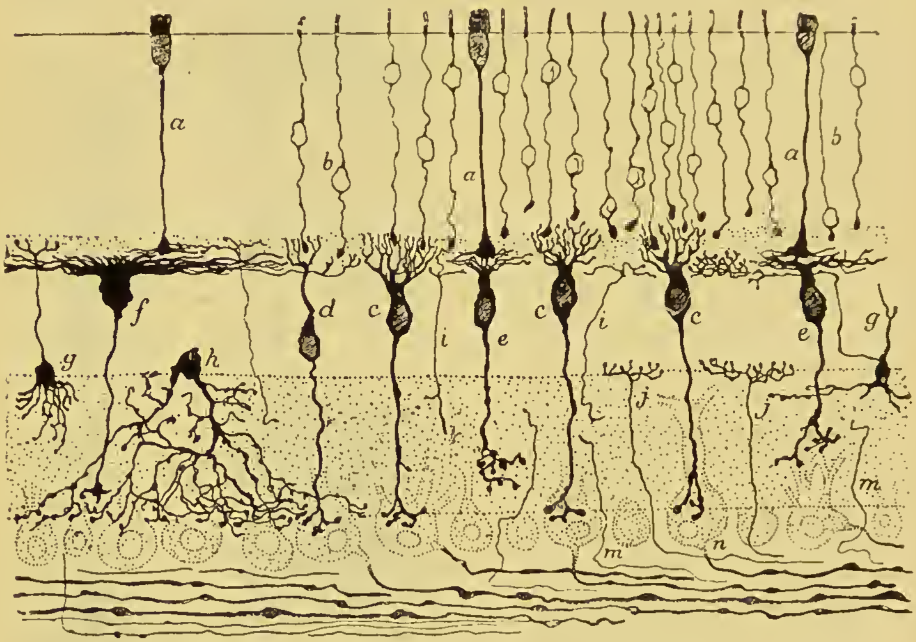

Fig. 333.—Section of Dog's Retina treated with Golgi's Method.

a, Cone-fibre; *b*, rod-fibre and nucleus; *c*, *d*, bipolar cells, their outer processes arborising round the enlarged ends of rod-fibres; *e*, bipolar cells with flattened arborisations for the ends of cone-fibres; *f*, giant bipolar with flattened arborisation; *h*, (spongioblastic) unipolar cell arborising in inner molecular layer; *i*, nerve-fibrils passing into outer molecular layer; *m*, nerve-fibril passing into inner molecular layer; *n*, ganglion cells.

nucleus and nucleolus surrounded by a little perinuclear protoplasm. The inner process of the cell passes into the inner molecular layer and breaks up into a network of fibres. It is the axis-cylinder of the cell, and generally reaches the inner part of the molecular layer in an undivided state. The outer or peripheral process is thick and short and penetrates the outer molecular layer, where it terminates in an arborescent manner. There are also unipolar cells. Of these, one set are arranged immediately below the external molecular layer. They are some-

what flattened or ovoid, with several processes which pass into the outer molecular layer. The other group of cells are smaller and more rounded and have processes which arborise in the inner molecular layer. The former are generally called "amacrine," and the latter spongioblastic cells.

(3) The *layer of rods and cones*, and the *rod- and cone-fibres and nuclei of the outer nuclear layer.*—The *rods* are much more numerous than the cones, except in the fovea centralis of the macula lutea—*i.e.*, in the visual axis of the eye. Each rod consists of an inner and an outer segment, of which the outer is cylindrical, transparent, and shows a tendency to break up into superimposed discs. It is also apparently slightly fluted longitudinally. The inner is somewhat spindle-shaped, and broader in its middle than the outer segment. Its outer part is composed of fine fibrils, while the inner is homogeneous or finely granular. The outer segment contains normally the visual purple or *rhodopsin*, which is bleached on exposure to light. While unstainable with hæmatoxylin or carmine, the outer segment readily stains with osmic acid. The inner segment, on the other hand, stains readily with hæmatoxylin, but not with osmic acid. Each rod, after piercing the external limiting membrane by its inner pointed extremity, is connected with a *rod-fibre*—a delicate varicose filament which traverses the outer nuclear layer and terminates in an *end-knob* in the outer molecular layer; the end-knob being imbedded in the arborisation of the outer process of one of the bipolars of the inner nuclear layer. Each rod-fibre exhibits at some part of its course an oval nucleus, which appears striped, from the arrangement of its chromoplasm. The *cones*, much fewer and shorter than the rods, are, like them, composed of an outer and inner segment, but are conical and not cylindrical. The outer segments are very small compared with the inner, and much smaller than those of the rods, which they apparently resemble in structure, without, however, possessing the visual purple. The inner segment resembles that of the rods, but is shorter and broader. After piercing the outer limiting membrane, the cone becomes connected with a *cone-fibre* (or we may say is continued as the cone-fibre) which extends to the outer molecular margin, where it expands into a kind of foot: this breaks up into branches, which come into relation with the arborisation of the peripheral process of one of the bipolar cells of the inner nuclear layer. A cone-fibre is much thicker than a rod-fibre, and contains a nucleus, generally placed just within the external limiting layer.

The molecular layers, inner and outer, are thus composed of the network given off from the fibres of Müller (neuroglial) and the arborisations of the nervous elements imbedded in a homogeneous ground substance.

3. The **pigmentary layer of the retina** is composed of cells which are hexagonal in outline when seen in surface view from the choroidal aspect. Externally, they are in contact with the

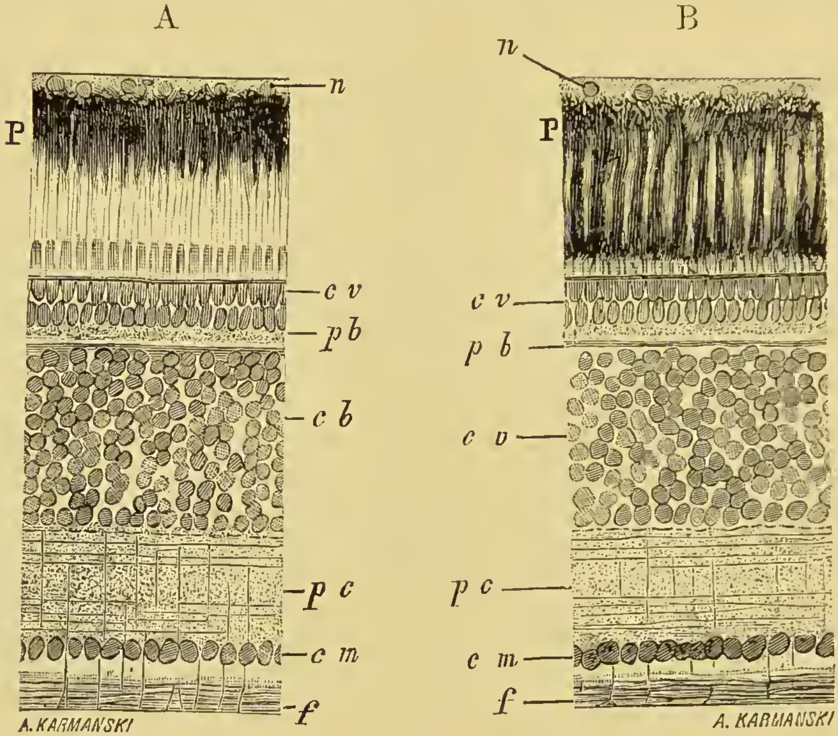

Fig. 334.—Vertical Section of Retina of Frog, showing the effect of Light and Darkness on the Pigment Cells.

A, Kept in darkness previous to hardening, showing pigment retracted. B, Exposed to light, showing pigment extending down between the rods. P, Pigment cell layer, with *n*, nuclei of cells; *cv*, outer nuclear layer; *pb*, outer molecular layer; *cb*, inner nuclear layer; *pc*, inner molecular layer; *cm*, ganglion cell layer; *f*, layer of nerve-fibres.

membrane of Bruch, and internally with the rod and cone layer of the retina. The inner surface of the pigmentary layer is always irregular, and either in contact with the ends of the rods and cones or drawn out into filamentous processes extending between them, in some cases as far as the membrana limitans externa. The processes pass down in this way if the eye be exposed to light, and are again retracted in darkness. "The

pigment appears to have, *inter alia*, the function of renewing the colour (visual purple) of the outer segments of the rods after these have become bleached from exposure to light." The outer part of the cells is often free from pigment, especially when the processes have been sent out. Each cell possesses a nucleus.

At the **macula lutea** the structure of the retina is different from elsewhere. The macula is oval in shape, its long axis being placed horizontally. It is about 2 mm. in this diameter, and is placed a little to the outer side of the entrance of the optic nerve. The outer raised rim is yellow in colour, but the colour is absent from the central depression or fovea centralis. The thickness of the margin of the macula is due to a large extent to the ganglion cell layer, in which the cells may be as much as eight or ten deep, though the other layers are also considerably thickened. As the fovea is approached the layers thin out, and in its centre only the cones, the cone-nuclei and fibres of the outer nuclear layer, and a thin representative of the remains of the inner nuclear layer and the neuroglial elements are left. If the rod and cone layer be traced inwards from the margin, the rods will be observed to become fewer in number and to be absent altogether in the fovea. The cones here exhibit a change in form, the outer segments becoming lengthened and thinner, while the inner segments remain unchanged. In the centre of the fovea the thickness of the retina is mainly due to the *cone-cells*, by this being understood the cones and the cone-fibres and nuclei.

Inter-communication of the retinal elements.—The only direct anatomical continuity between the nervous layers appears to be found between some of the nerve-fibres and the ganglion cells external to them. With this exception, the nervous elements come into relation with each other only by the interlacement of their arborisations, which takes place in the molecular layers. Thus, in the outer molecular layer the rod- and cone-cells come into relation with the bipolar cells of inner granules, and in the inner molecular layer these last with the ganglion cells. From without inwards three nervous strata or neurons may be traced: an *outermost* consists of the rod- and cone-cells, the peripheral ends of which project into or against the pigmentary layer, while their central ends in the outer molecular layer interlace with the arborisations of the peripheral processes of the bipolar cells of the *middle* stratum or inner nuclear layer. The bipolar cells, by their central ends in the inner molecular layer, interlace with the peripheral processes of the ganglion cells of the *innermost* stratum. Each ganglion cell possesses a central process which is the axis-

cylinder of a fibre of the optic nerve, and the terminal arborisation of these fibres is in the grey matter of the superior corpora quadrigemina or lateral geniculate bodies.

Visual function of the retina.—The sensitive layer of the retina is apparently that of the rods and cones. This is indicated in the first place by the fact that when this layer is absent no stimulation is possible. Thus the point of entrance of the optic nerve is insensible to light, and is termed the "blind spot." This can be readily demonstrated as follows:—If the page be held at a distance of about six inches, the right eye closed and the left directed to the cross, the spot will also be visible. On increasing the distance slowly the spot will suddenly disappear from the field of vision, and will as suddenly reappear if the distance be still further increased. That is to say, the spot disappears as soon as the position of the page is such that rays proceeding from it fall on the optic disc, and reappears as soon as they pass this area and fall on another part of the retina. We are ordinarily unconscious of the existence of the blind spot because the optic discs do not form

Fig. 335.—Mariotte's Experiment.

"identical points" in the two retinæ, so that one eye supplies or "covers up" the defect of the other: and also, as the blind spot does not lie in the line of distinct vision, it is readily neglected by the mind. In the second place, we can prove that the sensitive part of the retina lies behind the nerve-fibre and ganglion cell layers in which the main branches of the blood-vessels run. *Purkinje's figures* may be demonstrated by holding, in a dark room, a candle flame a little to one side of the eye, while vision is directed into the darkness. If the candle be moved slightly to and fro a branching figure of the blood-vessels is seen, which moves in the same direction as the candle, thus showing that the part of the retina which receives the stimulus lies behind or outside the vessels which cause the shadows. Further, from a knowledge of the angle of the incidence of the rays, the movement of the candle flame and its images, and the dimensions of the eye, it can be determined that the position of the sensitive layer corresponds with that of the rods and cones. Thirdly, that the rods and cones, with their fibres and nuclei in the outer nuclear layer, are the terminal sense-cells of the retina is indicated by the

fact that the macula lutea, in which the other layers become thinned out and in the centre almost absent, is the most sensitive part of the retina; and as the cone-cells are more numerous in the macula than elsewhere, and in the fovea only cone-cells are present, we may conclude that the cones are of more importance for distinct vision than the rods.

According to the above, in comparing the retina with other sense organs, such as the olfactory, we should regard the rod- and

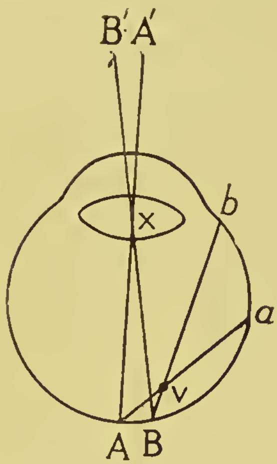

Fig. 336.—Diagram showing formation of Purkinje's Figures when the Illumination is through the Sclerotic.

The rays of light are concentrated with a lens on the outside of the sclerotic, behind the cornea. The light in this case comes from the spot *b*, and throws a shadow of the vessel *v* on the retina at B, and the shadow is seen in the field of vision at B′; if the light is moved from *b* to *a*, the shadow moves on the retina from B to A and is seen in the field of vision at A′.

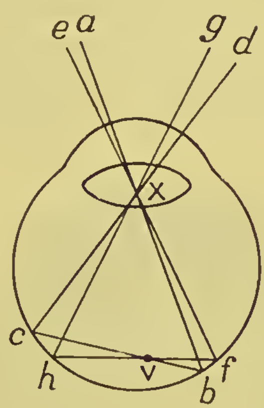

Fig. 337.—Diagram showing formation of Purkinje's Figures when the Illumination is through the Cornea.

The light *a* forms an image on the retina at *b*, and *the light reflected from this spot* casts a shadow of the retinal vessels *v* on to the retina at *c*, the image of the shadow being seen at *d*. If the light be moved from *a* to *c*, the shadow seen will move in the same direction from *d* to *g*.

cone-cells as corresponding to the olfactory cells. This is the most general view, and though it leaves the bipolar cells of the inner nuclear layer unaccounted for, it seems on the whole more satisfactory than the alternative view that the bipolars are themselves the homologues of the olfactory cells.

The precise way in which a ray of light stimulates the nerve-endings in the retina is at present obscure. It may be that the changes in form of the pigment cells when the eye is exposed to

light or placed in the dark are associated with the formation of photo-chemical substances which stimulate the terminal sense-cells. The behaviour of the visual purple or rhodopsin would favour such a view. If the retina of an animal which has been kept in the dark be excised in red light and examined in ordinary light it appears of a red purple colour, which becomes entirely bleached on continued exposure. If it be replaced in the dark the visual purple becomes renewed, provided the retinal epithelium is present; but if a frog be curarised the hexagonal cells separate from the rest of the retina. If the eye be now exposed to bright light, so as to bleach the retina, and this membrane be excised and placed in the dark, no regeneration of the visual purple takes place. Furthermore, if the retinal epithelium be lifted off an excised retina exposed to light, the purple is bleached; but if the retina be placed in the dark and the epithelium replaced, the colour is restored. Again, if while the retina as a whole is kept dark one portion be exposed to light, this only is bleached, and, if the eye be rapidly excised, the picture thus formed may be permanently fixed by alum, and is termed an "optogram." The rhodopsin can be dissolved out of the retina by a solution of bile salts, forming a deep purplish fluid, which bleaches on exposure to light.

Fig. 338.—Part of Retina of Rabbit, the Eye of which had been directed to an illuminated plate of glass bearing strips of black paper.

The visual purple, however, can scarcely be essential for sight, as it is absent from the fovea, where only cones are present, and is entirely absent from the retina of some animals, such as the pigeon, which undoubtedly is not normally troubled with indistinctness of vision. Nor, susceptible as the pigment cells are to the action of light, and intimately associated with the renewal of the visual purple as they seem to be, can they be regarded as themselves essential for vision, for albinos, in whom the pigment is absent, can see.

Light falling on the retina produces a change in its electrical condition, and it might at first sight appear that there had been a conversion of the energy of the rays of light to electrical energy, and that the stimulation of the retina was electrical. But the currents of action after all merely show that the retina has been excited, and this does not carry us far as to the *modus operandi.*

Acuteness of vision and sensibility in different parts of the retina.—The fovea centralis is the region of most acute or distinct vision, but it is not the most sensitive part of the retina, for it requires a higher minimal stimulus to produce excitation by white light than the part immediately around it. Apart from this, however, the sensibility of the retina may be said to become progressively less as we pass from the fovea outwards, and this applies to coloured as well as white light. When the field of vision is tested with the perimeter, it is found that white is perceived over the largest area, followed by the colours, in the order blue, red and green. The retinal rim is practically colour blind.

The *perimeter* possesses a graduated arc, as shown in the figure, which can be rotated through a circle, in the centre of which the eye to be observed is placed. The knob on the left is adjusted just under the eye of the patient, who looks forward along the line of the axis of the arc. A piece of white paper moved along the arc is the test object for white light. The arc is placed in any meridian, and the examiner determines the exact point on the arc at which the object ceases to be visible as it is moved towards the periphery of the field of vision. The point is recorded on a chart by a simple mechanical arrangement. The observation is then continued by placing the arc successively in different meridians, and recording in a similar way the points at which the object ceases to be seen in those meridians. The tracing is finally completed by joining the various points punctured on the chart. The field of vision is most extensive on the outer side because of the presence of the nose on the inner. Fig. 340 shows a perimetric drawing

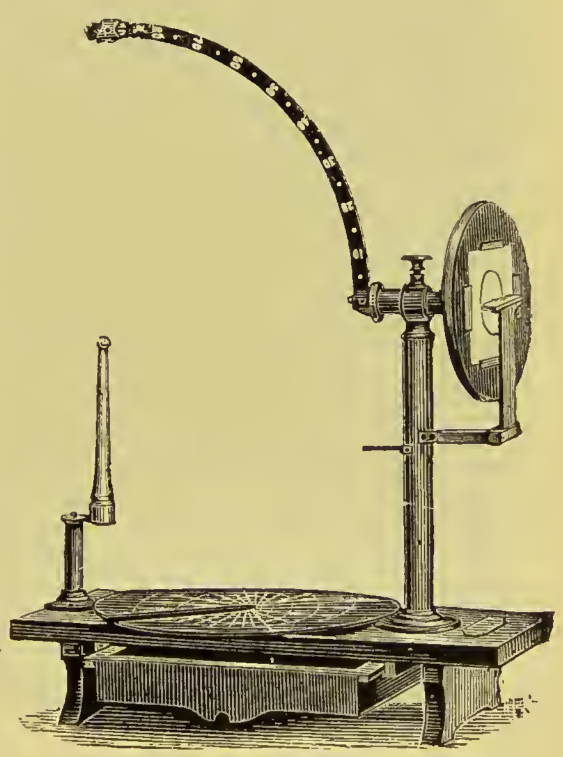

Fig. 339.—PRIESTLEY SMITH'S PERIMETER.

constructed in this way. The field for colour vision is mapped out in the same way, the test object being then coloured.

The sensitiveness of the retina not only varies with the area on which the light falls, but also with the general brilliance of the illumination. Aubert has shown that after light is completely excluded, the sensitiveness increases greatly, more especially in the first minutes, until after two hours the retina may be

Fig. 340.—Perimetric Chart of Right Eye.

The numbers represent degrees of the visual field measured on the graduated arc of the perimeter.

from twenty-five to thirty times as sensitive as when the eye is exposed to full illumination. Thus on going from a well-lighted to a darkened room, objects which are at first badly defined become gradually more and more distinct. The change is sometimes called dark-adaptation. In the case of colour perception, however, there is a marked difference. Certain colours, such as red and orange, which in bright light are peculiarly well-defined, are

quite indistinct in feeble light, whilst others, as blue and green, remain quite distinct. While the retina normally responds only to light rays, other forms of excitation may produce the sensation of light, such as electrical stimulation, mechanical pressure, &c. If gentle pressure be applied to the side of the eye—in a darkened room—coloured images are observed, which are termed phosphenes, and if the pressure be prolonged flickering lights may appear, or curiously figured images.

Conditions necessary for a double impression.—The spaces between the cones in the fovea centralis are necessarily insensible to light. If images of two small points fall on the retina they will be distinguishable as separate images, provided they fall on separate cones, and in order to do this they need only be 3 to 4 or 5 μ apart, for then they may still fall on two adjoining cones. If the distance be sufficiently less for both the images to fall on one cone, or one on one cone and the other on the interconal cement substance, only one image is perceived. The peripheral part of the retina is less sensitive in this respect, the images requiring to be further apart to secure a double impression.

Duration of the stimulus.—The time necessary for stimulation of the retina is exceedingly small, a flash of lightning being practically instantaneous, or lasting, say, $\frac{1}{1000000}$ of a second. But though the stimulus in this case is of so brief a duration, the impression produced is by no means so, for it always lasts about one-eighth of a second. Thus an object in motion seen by a flash of lightning appears stationary, because, although the retinal *impression* lasted for an eighth of a second, it by no means follows that the stimulus lasted for that time. On the contrary, the stimulus lasted for so infinitesimal a period that no appreciable movement was possible. That the impression survives the stimulus which causes it is readily demonstrated by *fusion of impressions.* If a wheel be rotated sufficiently rapidly the individual spokes are not distinguishable. This is because the impression caused by one spoke has not faded away before another spoke occupies the position previously held by the first, and renews the stimulus. The cinematograph, &c., are excellent examples of the phenomenon; a second picture being presented to the eye before the image of the first has faded away. The fusion of retinal stimuli may be compared with the tetanisation of muscle.

After-images.—This form of after-sensation is of two kinds—positive and negative. Positive after-images resemble the real ones; in negative after-images the lights and shadows are reversed. Thus, if after looking for some time at the window panes through

which a bright light is streaming we close the eyes, a reverse picture may be seen in which the panes are dark and the bars light. This is a negative after-image, and the reversal is said to be due to the exhaustion of the parts stimulated. Positive after-images are formed when the stimulation is of shorter duration, as when the sun is looked at momentarily and the eyes then closed, or a burning stick is revolved rapidly, when there is the appearance of a continuous circle of fire. This phenomenon, which is due, as in the case of the spokes of the revolving wheel, to the impression surviving the stimulus, is also an instance of a positive after-image.

The **Ophthalmoscope.**—Under ordinary conditions it is impossible to see inside the eye. This is due partly to the absorption of the rays by the retinal pigment, but mainly to the fact that the head of the observer must be situated between the observed eye and the source of light, and thus prevents the entrance of the illuminating rays. When the ophthalmoscope is used, however, the observer's eye, though in the line of the incident rays, does not interrupt them. The first ophthalmoscope, as devised by Helmholtz, consisted of a series of superimposed glass plates (Fig. 341, SM). From the surface of these the light from an adjacent candle can be reflected into the observed eye, while the observer looks *through* the plates in the line of the illuminating rays. If A is the eye of the observer, B that of the observed, and x the flame from which the light is reflected, then the rays of light from x striking the plates SM are reflected into the eye B, the fundus of which is illuminated by diffusion circles round F; and the observer can see this illuminated area, as his line of vision is the same as that of the rays reflected from it.

The more modern form of the ophthalmoscope is merely an adaptation of the same principle, the observer looking through a hole in the centre of a concave mirror, which takes the place of the glass plates. When the *direct* method of examination is employed the mirror is close to the observed eye, the two eyes (of observer and observed) being only two or three inches apart. A magnified erect virtual image of a small part of the fundus is seen. When this is the case the rays proceeding from a point in the retina of the observed eye leave the eye as parallel rays, and are brought to a focus on the retina of the observer. If the eye of the observed is myopic the rays leaving it are convergent, and a biconcave lens requires to be placed in front of the observer's eye in order to obtain clear vision; similarly, if the observed eye is hypermetropic the rays leaving it will be divergent, and the

unaccommodated eye of the observer will require the help of a biconvex lens to render them parallel.

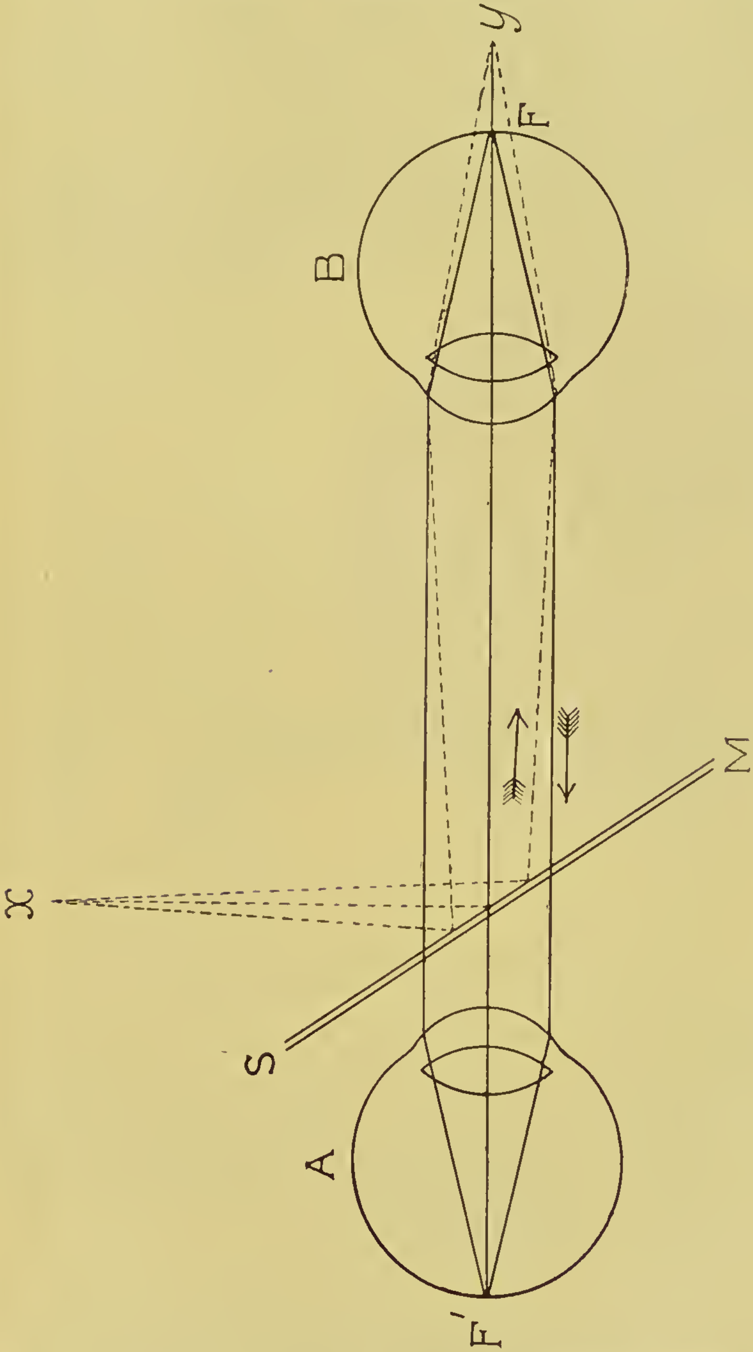

Fig. 341.—PRINCIPLE OF OPHTHALMOSCOPE.

A pencil of rays from x are reflected from plate SM and focussed at y behind the retina, thus illuminating a portion of it. Rays from a point in this portion, F, will be focussed at F' in A, if A be normal.

Anomalies of refraction in the refractive media of the eye may be determined and measured in this way, the ophthalmo-

scope being provided with a series of *plus* and *minus* lenses for placing before the eye of the observer, who, in his examination, must keep his own eye unaccommodated. Solution of atropin may be applied to the observed eye to paralyse accommodation and dilate the pupil. The observer must allow for any defects of refraction in his own eye.

When the *indirect* method is used the mirror is held at the ordinary visual distance of ten inches, a convex lens is held two or three inches in front of the patient's eye, and the light reflected through it. In this case a real inverted aerial image, formed between the lens and the observer's eye, is obtained of a larger

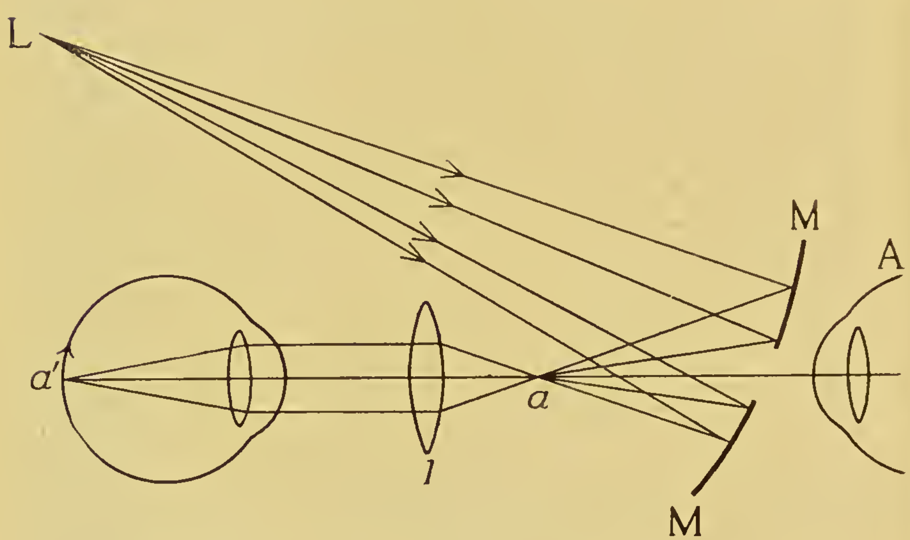

Fig. 342.—The Ophthalmoscope (Indirect Method).

part of the fundus than was seen by the direct method, but it is less magnified.

Fig. 343 illustrates such a view of the optic disc with its central pit, and near the centre the arteria centralis retinæ and its accompanying vein emerging from the optic nerve and breaking up into branches. To the right is shown the yellow spot with the blood-vessels sweeping round it.

Colour sensations.—We have seen that when a beam of light passes through a prism it is bent at both surfaces towards the base, but it also undergoes dispersion, the rays of shorter wavelength being more refracted than those of longer. This is what

takes place when ordinary white light passes through the prism of the spectroscope; instead of the rays of unequal length being intermingled, as they ordinarily are, they are separated, sorted out as it were, and arranged in series in the order of their refrangibility. The red rays are at one end of the spectrum and the violet at the other, with orange, yellow, green, blue and indigo between. The red rays are the longest and least refrangible, the violet the shortest and most refrangible. The difference in the colour sensations produced by the various rays depends on differences in the rate of the vibrations producing the rays, the red being the least rapid and the violet the most.

Fig. 343.—Fundus of Eye as seen by Indirect Method.

But, in addition to the colour rays, white light contains others which do not stimulate the retina. The dark heat rays which are refracted least lie to the left of the red in the spectrum, while the actinic, or chemically active rays are refracted most, and lie beyond the violet.

It is not, however, found that all the colour rays of the spectrum are required to produce the sensation of white light. Thus an admixture of red with bluish-green rays will produce the sensation of white, and the same is the case when orange and blue, or yellow and violet are combined. These pairs are called "complementary" colours, and their relation to each other is shown in the accompanying colour table (Fig. 344).*

Colours are commonly defined by their qualities of—(1) *Tone* or *hue*, *e.g.*, red, blue, &c., this depending on the rapidity of the vibrations of the ether; (2) *purity* or *saturation*, and this depends

* The effect of mixing colour sensations is conveniently demonstrated by causing the colours to fall on the retina in rapid succession. This may be accomplished by fixing coloured sectors to a disc, which is then caused to revolve rapidly. As the retinal impressions survive the stimuli causing them they become blended, as in the case of the spokes of the rapidly-rotated wheel.

on freedom from admixture with other colour sensations or white light. Thus, if blue rays be mixed with white light the result is a pale or unsaturated blue, and the result is the same if the blue be mixed with its complementary colour (orange), provided the blue be in excess of what is required for the production of white light, the sensation being one of pale blue. If the proportion of blue be increased, the resulting sensation approaches more nearly the saturated blue of the spectrum; (3) *brightness* or *intensity*—the degree to which the sensory mechanism is stimulated by the rays.

According to the **Young-Helmholtz theory** of colour vision, there are in the cerebro-retinal organisation three sets of elements, or more probably three photo-chemical substances, which may be termed red, green and violet, as they are respectively most

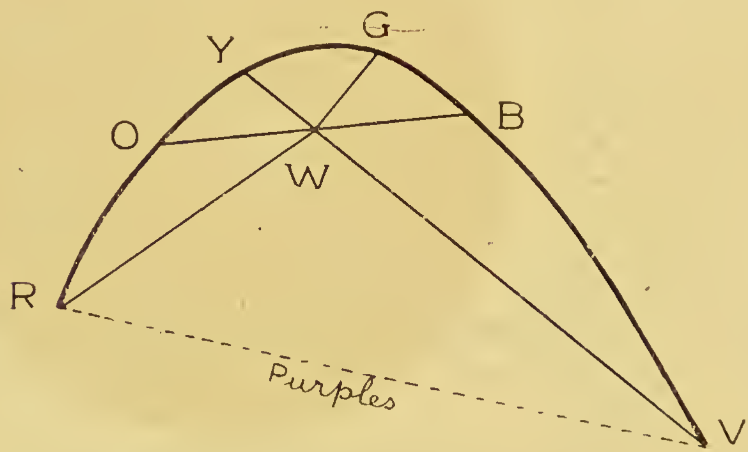

Fig. 344.—Geometrical Colour Table.

excited by the rays producing these sensations. Thus the red elements respond most to waves of considerable wave length (red), to a less extent to medium waves (green), and to a still less extent to the shortest waves (violet). The green elements respond most to waves of medium length (green), and to a less extent to the longer and shorter waves (red and blue). The violet elements are excited most by the shortest rays (violet), less by the medium (green), and still less by the long (red). This supposition enables us to explain apparently satisfactorily the production of white light when complementary colours are mixed, for in such a case the three elements are stimulated in the proportion required for the sensation of white light. According to the theory, red, green and violet represent the three

primary colour sensations, from the admixture of which the sensation of white light results, the other colours being merely mixtures of these. Thus orange and yellow are mixtures of red and green in different proportions, blue of green and violet; and when orange is added to its complementary colour (blue), we obtain the sensation of white light, because orange is a mixture of red and green, while blue is a mixture of green and violet. We are, in other words, merely mixing the three primary colours.

Many of the phenomena of colour vision are readily explained by Helmholtz's theory. Thus, if the eye be fatigued for red and then exposed to a yellow light, the light assumes

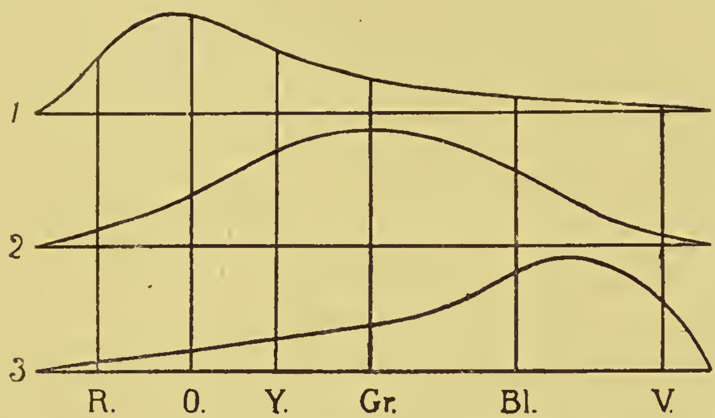

Fig. 345.—Diagram of Three Primary Colour Sensations.

1, Red; 2, green; and 3, violet primary colour sensations. The lettering indicates the colours of the spectrum. The height of the curves shows the extent to which the several primary sensations of colour are excited by vibrations of different wave length.

a green tinge, because, the red element in the cerebro-retinal system being exhausted, stimulation of the green element predominates. Similarly, if the eye be fatigued for green, and a blue light be looked at, the blue deepens to a violet, as the violet stimulation then predominates over the green. If the eye be fatigued for yellow light to the point of yellow blindness, it becomes blind to the red and green rays also, and this is in accordance with the theory that the sensation of yellow is a mixture of red and green sensations: and it is found that fatigue exhibits itself in the three "primary" colours—red, green and violet.

Again, according to Helmholtz's view that the red rays stimulate not only the red elements but also to some ex-

tent the green and blue, we should expect to find that the spectral colours, though physically saturated, are not physiologically so, and this is the case. If the eye be fatigued for bluish-green, and the red end of the spectrum be then looked at, it appears of a purer, more saturated red than before; the reason being that through the fatigue of the blue and green elements they are less excited by the red rays than they would have been if the red had been examined first, and hence the proportionate stimulation of the red elements is the greater.

After-images.—If a white disc on a black ground be looked at sufficiently to cause fatigue, and the eye be then directed to a white ground, a darkened image of the white disc is seen, and this is the ordinary negative after-image. Its production is due to the fact that in the area of the retina which received the rays from the white disc, the three elements are fatigued, and so respond less to the stimulation from the general white ground in the latter part of the experiment than the elements in the retina surrounding the area. Coloured after-images on a white ground appear in their complementary colour. Thus, if the eye be fatigued for red, a greenish-blue after-image is seen, as, the red elements being exhausted, white light will stimulate mainly the green and violet elements.

Hering's theory supposes that there are six primary colour sensations, viz., red, yellow, green, blue, white and black, and assumes the existence in the cerebro-retinal apparatus of three substances, the red-green, the blue-yellow, and the white-black. Each of these substances, corresponding to a pair of colours which are antagonistic and complementary, is capable of undergoing disintegration and reintegration. In the case of the white-black substance the sensation of white is associated with the process of destruction, the sensation of black with that of construction. Similarly, red and yellow sensations are associated with destruction, green and blue with construction of the respective hypothetical substances. The white-black substance is affected by all the rays of the spectrum acting together. If the amount of light be small, construction prevails over destruction, and the sensation is black; if it be great, destruction prevails over construction, and the sensation is white; when the two influences are balanced the sensation is grey. The red-green substance undergoes constructive changes under the influence of green rays (green sensation), destructive changes under the influence of red rays (red sensation). The blue-yellow substance is decomposed by yellow rays (yellow sensation), and built up again by blue rays (blue sensation) When the colour

influences of integration and disintegration are balanced the sensation is *nil.*

Phenomena of Simultaneous Contrast.—If a grey disc occupy the centre of a green ground, and the whole be covered by a layer of translucent tracing paper, the grey disc appears in the complementary colour of the ground, viz., purple-red.* This is apparently because the fatigue of the green elements produced by the green ground has extended inwards and thus the part of the retina† stimulated by the grey disc (white light) responds mainly to the purple-red rays. Similarly, a grey disc on a red ground will appear green, on blue background yellow, &c. Helmholtz maintained that the phenomena was of cerebral origin—namely psychical; while Hering ascribes it to an integrative or disintegrative process set up in the portions of the retina contiguous to the part stimulated by the colour: thus while the red background katabolises the red-green substance, there is an anabolic process set up in the central part, giving the grey disc a green colour. Recent experiments by Sherrington and others would, however, seem to prove that the contrast phenomena have a peripheral or retinal origin, and not a cerebral, as Helmholtz believed. All portions of the retina are not equally sensitive to ordinary and coloured light. The visual acuity diminishes as we pass away from the central to the peripheral parts. The variation is, however, most marked in colour sense. The central portion of the retina seems to respond to all colour rays—or possesses full colour sense; externally lies a mediate zone in which the sensitiveness to red and green is much diminished; and, lastly, a peripheral area which is non-sensitive to all colour. This is not quite accurate, however, as the peripheral zone can distinguish tints if the intensity of the colour be sufficiently increased. It is also very interesting to note that a coloured object changes in tint as its image passes from the centre to the periphery of the retina. Red and green colours first become blue and yellow and then become colourless; on the other hand, blue and yellow colours do not change in tint, though they gradually become less distinct. As the cones are in marked evidence in the central portions of the retina, where colours are most accurately perceived, it is very frequently held that they have to deal, not only with ordinary sensation (visual), but also with colour sense, and that the rods which occur in great excess at the periphery, where colour sense is very feeble or absent, are concerned more

* Green has no simple complementary colour in the spectrum, its complementary colour would lie amongst the purple, indicated in the colour triangle by a dotted line.

† "Retina" is here used loosely to signify the nervous visual apparatus.

especially in the perception of luminosity. Von Kries maintains that the cones are the more highly specialised terminals, and are concerned chiefly in the perception of colour rays and the localisation of definite visual stimuli, and that the rods, on the other hand, while more sensitive to rays of feeble luminosity, are not particularly responsive to colour. Further, the rods seem to possess a remarkable power of adaptation to variations in the intensity of the light. It is impossible, however, to reconcile with either theory all the phenomena of colour vision, and one of these, the condition known as colour-blindness, requires mention.

Colour-blindness may be congenital or acquired. It may also be *complete*, in which there is an absolute inability to distinguish between any colours, or *incomplete*, where there is interference with a complementary pair, such as red and green or blue and yellow.

Of colour-blindness, the commonest form is red-green blindness, the sufferer being unable to distinguish properly between red and green. According to Helmholtz's theory, this is due in the red-blind person to the absence of the red element, and in the green-blind person to the absence of the green element. But such persons experience the sensation of white light, and according to the theory this should necessitate the presence of all three elements. Even if we allow that the stimulation of the remaining two elements only may produce the sensation of *what is white light to the patient*, we are not yet "out of the wood," for a doubly colour-blind person who can only see blue is still sensible of white light, and this should be impossible, as according to the theory he has only one of the three elements left, and stimulation of this alone could not result in the sensation of white light. According to Hering's theory in the red and green blind, the red-green substance is absent, but here again a difficulty arises; for there should thus be no difference between the two forms of colour-blindness—red and green. But there is a great difference, and the theory is clearly insufficient. The perception of white light by the colour-blind is, however, readily understood by Hering's theory, for the white-black substance still remains.

Single vision with two eyes.—A separate image of any object looked at is of course formed on each retina, and yet under ordinary conditions the mind only perceives a single image; that is to say, the two images are in our consciousness blended into one. This is explained by the *theory of identical points*. According to this theory, each point in either retina corresponds to a point in the other, and when simultaneous images of an

object fall on the corresponding points of the two retinæ, the mind refers these images to one point in space. We may find the identical points in each retina if we suppose (the eyes being

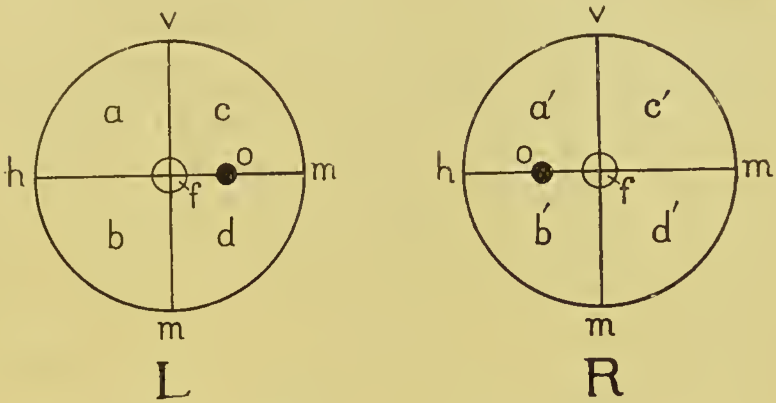

Fig. 346.—Corresponding Parts of Retina.

a, *b*, In temporal side of left retina correspond to *a′ b′* on nasal side of right retina; *O*, blind spot; *f*, fovea; *vm*, *hm*, lines of separation.

in the primary position) one retina to be exactly superimposed on the other, as a couple of plates might be, fovea corresponding with fovea. Then each point in either membrane will be covered by the corresponding point in the other. A little consideration will show that the temporal half of one retina will correspond with the nasal half of the other, and that the two blind spots are not identical points. This correspondence between the nasal half of the retina with the temporal half of the other is closely related to the course of the fibres of the optic nerve at the chiasma. From the accompanying figure it will be seen that the decussation

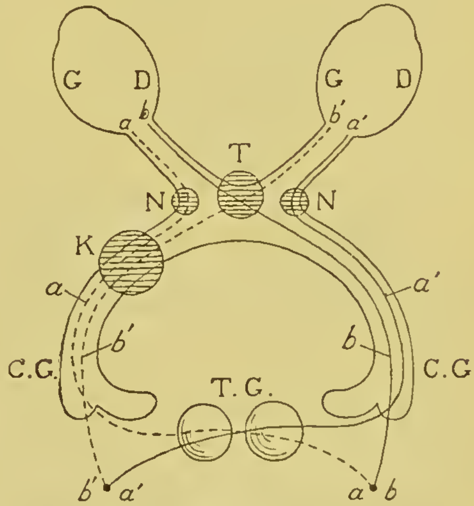

Fig. 347.—Diagram of Decussation of Optic Tracts.

T, Semi-decussation in chiasma; *T.G.*, fibres passing through the corpora quadrigemina; *aa′*, temporal fibres; *bb′*, nasal fibres; *C.G.*, corpora geniculata.

of the fibres is incomplete, only those from the nasal side of each retina crossing over. Hence the fibres from the nasal half of one eye and the temporal half of the other come into relation with the same side of the cerebral cortex. If one eye be gently rotated, so that the retinal image of some external object is not formed on corresponding points, a double mental image is at once obtained.

The surface in the outside world from which images may fall on identical points in the two retinæ is termed the *horopter*, and this surface will vary with the direction of the visual axis. The positions of the eyeballs are named primary, secondary and tertiary.

Primary.—Visual axes parallel, visual plane horizontal.

Secondary.—(1) Visual axes parallel, visual plane directed upwards or downwards; and (2) visual axes convergent, visual plane horizontal.

Tertiary.—Visual axes convergent, visual plane directed upwards or downwards.

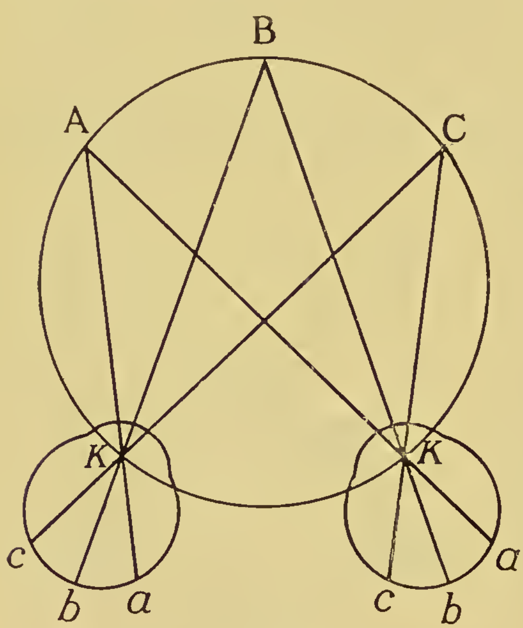

Fig. 348.—Diagram of Horopter when the Visual Axes are Convergent.

When the visual axes converge at B, the images of points A and C in the circle through B and the nodal points KK will fall on corresponding points.

When the visual axes are parallel, as in looking at the horizon, the horopter is a plane in infinity. When the axes are convergent, as in the second variety of the secondary position, the horopter consists of a circle which passes through the nodal points of the two eyes and through the fixed point to which the gaze is directed, and of a straight line through the fixed point at right angles to the visual plane. Fig. 348 shows the circular horopter, in which B represents the fixed point at which the gaze is directed, and *bb* the two yellow spots, which are identical points.

A and C, points in the circle, reflect images which fall on identical points on the two retinæ: a being identical with a, and c with c. Such points in the horoptic circle are seen singly. That rays from other points will fall on parts of the retinæ which are not identical, and so give a double image, may be readily understood by reference to Fig. 349. Let ABC be three points in a line towards which vision is directed, then abc and $a'b'c'$ will be corresponding points in the retinæ. But rays coming from X, nearer than ABC, or from Y, further away than ABC, will *not* fall

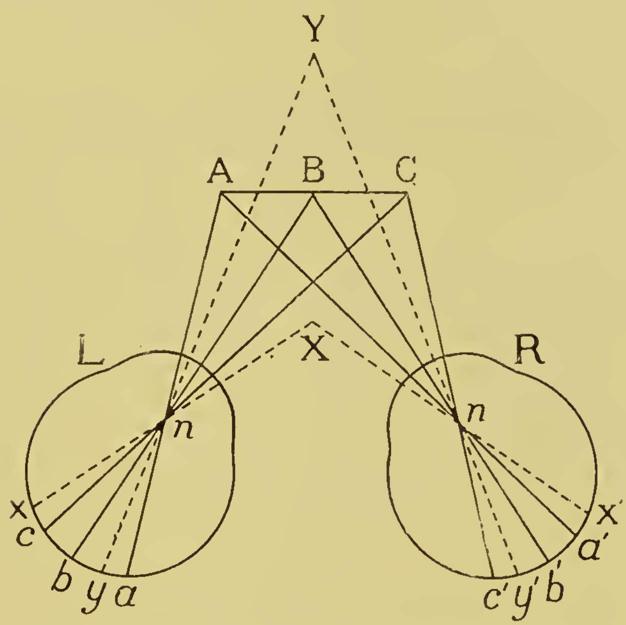

Fig. 349.—Diagram Illustrating Corresponding Points.

n, Nodal point; b, fovea. The points a' b' c' in the right eye correspond to a b and c in the left eye. But the points x' and y' in the right eye do not correspond to x and y in the left.

on identical points. This is shown in the figure, for xx' fall on the temporal and yy' on the nasal side of each retina. Now, the temporal half of one retina does not contain points identical with those in the temporal half of the other, but in the nasal, and *vice versa*.

All objects then, the rays from which fall on non-identical points, appear double, but though a very large number of these double images must be formed, they are not consciously perceived by us. One reason for this is that the attention is always

specially concentrated on the point in the field of vision at which the visual axes intersect, *i.e.*, the point to which the gaze is directed, and for which the eye is accommodated. Rays from this point of course fall on identical points, *i.e.*, on the fovea of each retina. Again, as we pass outwards from the fovea the retinal impressions become less distinct and are thus the more readily neglected. Further, though rays from an object may not fall on mathematically identical points, the two images may fall on areas which overlap physiologically, and this is especially liable to be the case in the peripheral parts of the retina where the identical points increase in area, in which case the two images are blended into one.

Visual judgments.—We estimate the apparent **size** of an object according to the size of its retinal image, or what is the same, the visual angle under which it is seen. But, inasmuch as we know that the size of the retinal image varies directly with the size of the object, but inversely with the distance of the object from the eye, the element of distance enters largely into our calculation of the actual size of the object. Thus, in looking through the window at a building some little way off, we may find that the diameter of one of the glass panes corresponds exactly with that of the building, and though the diameter of the retinal images will be the same, and of course the visual angle also, we do not estimate the size of the window pane and the building as the same, because we *allow for distance.* We conclude that an object at the distance of 100 yards which will form an equal visual angle with one at a distance of three feet will be of a much greater size, and our *experience*, which is vast in such matters, enables us to form a fairly accurate conception of the size of the building without working out a mathematical sum. Our judgment of size, however, is very liable to err when the object looked at is a long way off, as we may easily under-estimate or overestimate the distance.

Just as our judgment of the size of an object is affected by its distance, so is our judgment of **distance** affected by apparent size. If we look at two similar chairs in a gallery, one three or four feet from us and the other some twenty or thirty, we estimate the latter to be the more distant because it gives the smaller retinal image, and we estimate the difference in the distance by the difference in the retinal images. When the retinal images of two objects are of the same size we estimate the distance by the amount of accommodation required, and in binocular vision by the amount of convergence of the visual axis also, the latter

being proportional to the contraction of the ocular muscles. The nearer the object, the greater the accommodation required, and the more marked the convergence of the visual axes.

We are also aided in our judgment of distance by the clearness or the contrary with which objects are seen, their position relative to other objects, &c. Our judgment in any case is really the result of experience acting upon us unconsciously, *i.e.*, we *learn by experience* to associate certain phenomena with distance and others with proximity. This element of experience is especially required for the proper perception of solid objects. Our estimation of **solidity** and the **form** of solid objects depends essentially on the conclusion we arrive at from the simultaneous presentment to the mind of two images of the object seen from different points of view. It is obvious that a plane surface will project identical images on the two retinæ, and, conversely, when

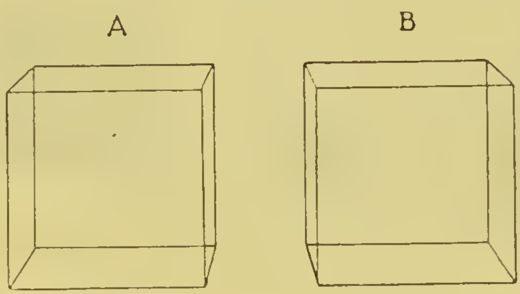

Fig. 350.—Diagram of a Cube seen from the Point of View of Either Eye.

the images are identical the impression will be that of a plane surface. It is only when the object looked at possesses three dimensions that the two images differ. When we look at a cube held before the eyes in the median line, the image seen by the left eye will be as at *A*: for from the relative positions of the eye and the cube we shall see a little of one side and it may be a perspective view of the top. Similarly, the image seen by the right eye will be as shown at *B*, because for the same reason we shall see a little of the opposite side of the cube this time and the top in different perspective. When two such images fall on identical points in the retinæ they are blended into one in our consciousness; and that image is not a plane one, but the object is seen projected in relief. It is on this principle that the stereo-

scope is based. When we use this instrument we do not look at identical pictures, which would only give a plane image. The photographs are taken one from the point of view of one eye, and the other from that of the other; and when these two images are superimposed in the cerebro-retinal apparatus, the resultant impression is that of the solidity which the subject of the photograph itself presented. Thus the solid form of an object looked at is constructed by the mind from the different perspective views of it obtained by the two eyes. The two pictures of a stereoscopic slide cannot, however, be interchanged. When that seen from the right is placed on the left, and that seen from the left on the right, the projections become hollows, while the depressions stand out in relief.

It is clear that there are difficulties in reconciling the results of stereoscopy with any mathematical insistence on the theory

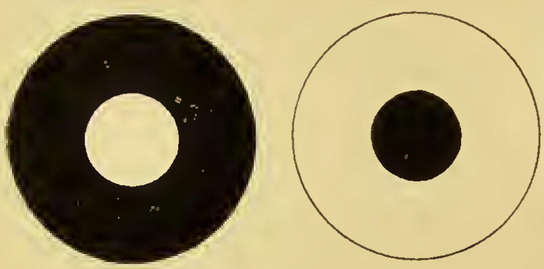

Fig. 351.—Irradiation.

Fig. 352.—Irradiation.

of identical points; for in the two stereoscopic pictures it is plain that many points will become superimposed, which, accurately speaking, do not fall on identical points. We must be content to say that those points are, at least physiologically if not anatomically, identical which by simultaneous stimulation give rise to a single image. If the differences between the two pictures be sufficiently great, however, the stereoscopic effect ceases; in other words, the mind (?) does not succeed in blending the images so far apart.

Error in judgment may be produced in many ways. Thus if we look at a white circle on a black ground it appears considerably larger than a similar black circle on a white ground. Again white squares are apparently larger than black ones, &c.

Again, error may be easily induced by the presence of outside factors—thus the horizontal line 1 appears longer than 2.

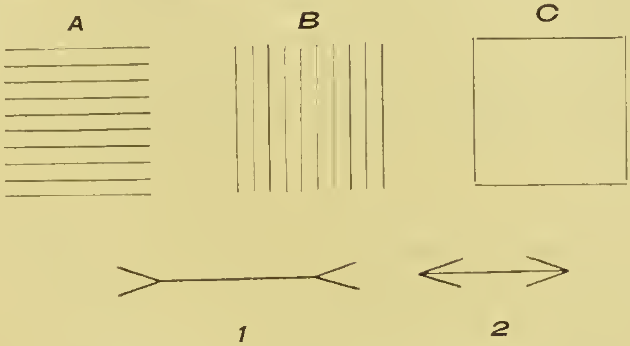

Fig. 353.—Illusions of Space-Perception.

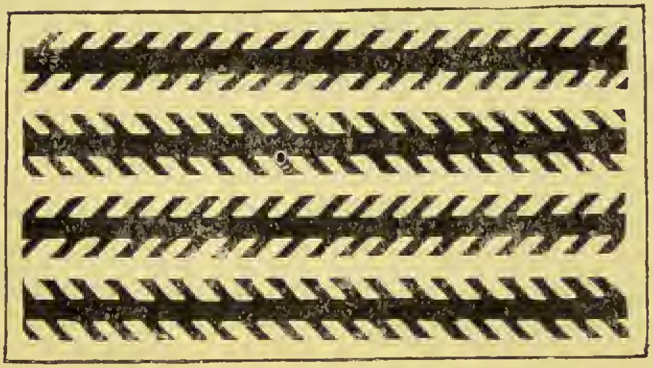

Fig. 354.—Illusion of Parallel Lines.

Movements of the Eyeballs.

The extrinsic muscles of the eyeball are the internal and external recti, the superior and inferior recti, and the superior and inferior oblique. The movements of the eyeball take place round the *point of rotation*, which is situated 1·77 mm. behind the centre of the visual axis. With the eyes in the primary position, the *antero-posterior axis* corresponds with the *visual axis*, and unites the vertex of the cornea and the fovea centralis. The *transverse axis* is formed by joining the two points of rotation, and continuing the line outwards. The *vertical axis* cuts the point of rotation at right angles to the other two. We may thus suppose three planes passing through the eyeball—a horizontal one, the plane of the visual axis,

which divides the eyes into upper and lower halves; a vertical plane (antero-posterior), in which the vertical and visual axes lie, dividing the eye into an inner and an outer half; and an equatorial plane (transverse), in which the vertical and transverse axes lie, dividing the eyes into anterior and posterior halves. The straight line which joins the fixed point in the outer world and the point of rotation of the eyeball is called the *visual line*, and the plane in which the two visual lines lie is called the *visual plane*.

From the primary position the eyeballs can be rotated upwards or downwards round a horizontal axis, inwards or outwards round the vertical axis, or upwards and inwards, upwards and outwards, downwards and inwards, downwards and outwards, round oblique axes which always lie in the same plane as the vertical and horizontal axes of rotation (Listing's law). Rotation round the visual axis occurs to some extent when the eyes are converged, and especially if they are directed downwards at the same time. The following table shows the part taken by the ocular muscles in the different movements of the eyeballs:—

Movement.	Muscles concerned.	Movement.	Muscles concerned.
Inwards.	Rectus internus.	Inwards and Downwards.	Rectus internus. Rectus inferior. Obliquus superior.
Outwards.	Rectus externus.		
Upwards.	Rectus superior. Obliquus inferior.	Outwards and Upwards.	Rectus externus. Rectus superior. Obliquus inferior.
Downwards.	Rectus inferior. Obliquus superior.		
Inwards and Upwards.	Rectus internus. Rectus superior. Obliquus inferior.	Outwards and Downwards.	Rectus externus. Rectus inferior. Obliquus superior.

From this it will be seen that in the simple lateral movements (inwards and outwards) the action of only one pair of muscles—the internal and external recti—is involved; for movements upwards and downwards two pairs of muscles are required; while the more complex movements in two directions necessitate the use of three pairs of muscles.

In studying the action of the muscles of the eyeball, we must note that the rotation caused by any individual muscle will take place round an axis represented by a line passing through the common point of rotation at right angles to the plane of traction of the muscle. The *plane of traction* passes through the middle of the origin and insertion of each muscle and the point of rotation of the eyeball. Accordingly, the internal and external recti rotate the eye about the vertical axis in the primary position. The superior and inferior recti rotate about an axis in the horizontal plane in the primary position, an axis which makes an angle of about 20° with the transverse axis. This axis of the superior and inferior recti is shown at *b* in Fig. 355, and it will be seen that there will be some inward rotation accompanying the main action of either muscle upwards or downwards. The axis of the superior and inferior oblique muscles also lies in the horizontal plane but makes an angle of about 60° with the transverse axis as seen at *a*: the superior oblique directing the eye outwards and downwards when it acts alone, and the inferior oblique directing it upwards and outwards. Now, according to Listing's law the eyeballs can only rotate from the primary position around axes that lie in the same plane as the vertical and horizontal axes of rotation, so that when the axes of the muscles do not correspond with these axes a compensating influence must be brought into play. Thus rotation upwards is brought about by the superior rectus and inferior oblique; rotation downwards by the inferior rectus and superior oblique. Oblique movements involve the action of a muscle of each of the three pairs.

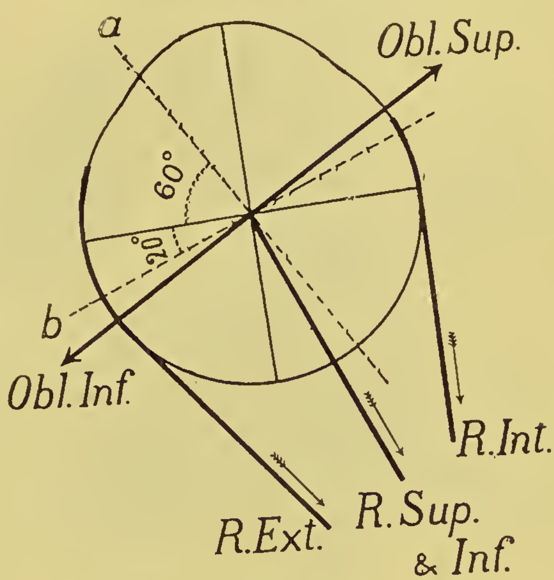

Fig. 355.—Extrinsic Muscles of the Left Eyeball.

The thickened lines show the direction of the pull of the muscles, the dotted line *a* the axis of rotation of the oblique muscles, and the dotted line *b* the axis of rotation of the superior and inferior recti.

The Sense of Hearing.

The organ of hearing consists of three parts—external, middle and internal, of which the two former are concerned with the conduction of sound, while the latter is receptive, and contains the terminations of the auditory nerve. Just as the transverse ethereal vibrations passing through the various media

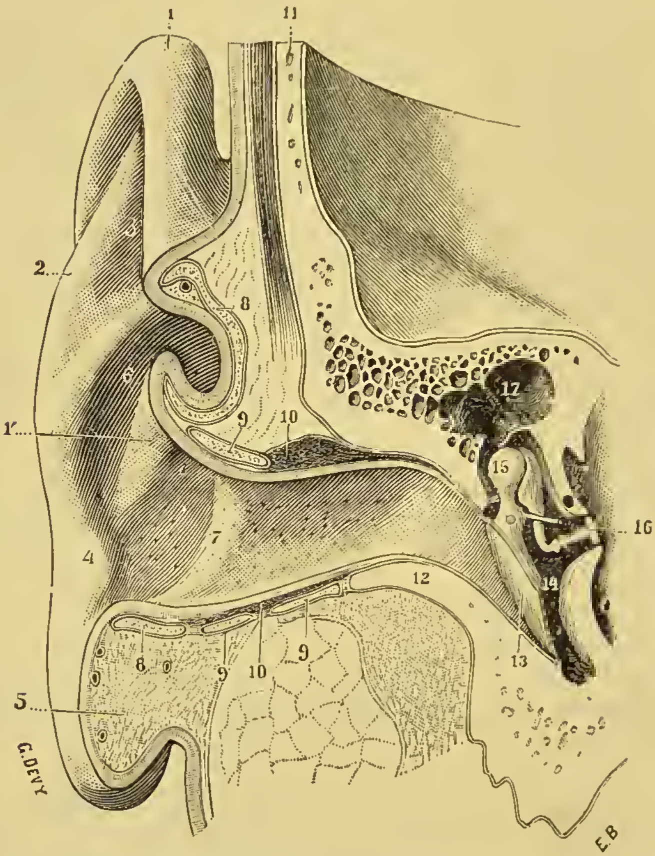

Fig. 356.—Parts Composing the Organ of Hearing of Right Side, seen from Before.

1, 2, 3, 4, 5, Parts of pinna of external ear; 7, entrance to external auditory meatus; 11, 12, temporal bone in section; 13, membrana tympani; 14, is placed in the cavity of the tympanum or middle ear, opposite the summit of the funnel-shaped membrana tympani, and the end of the handle of the malleus; 15, the head of the malleus; 16, the foot of the stapes filling in the fenestra ovalis.

of the eye stimulate the sense endings of the optic nerve in the the retina, so the longitudinal waves of rarefaction and condensation imparted to the air by vibrating solid or liquid bodies

impinge on the membrane of the tympanum, and are conducted by the ossicles of the middle ear to the lymph of the membranous labyrinth of the inner ear, and thus to the nerve terminations of the cochlea.

The **external ear** consists of the *pinna* projecting from the side of the head and the *external auditory meatus* leading from it to the tympanum or middle ear, from which it is separated by the *membrana tympani* or tympanic membrane. This is of the shape of an elipsoidal disc, and is fixed obliquely into the bone, its external surface looking downwards and a little forwards. It is not stretched flat, butprojects inwards like a funnel, the apex of the funnel corresponding with the end of the handle of the malleus, which, as we shall see, lies upon its inner or tympanic surface. In structure it consists of three layers, the external of which is formed by a prolongation of the skin of the external auditory meatus, while the inner is a reflection of the mucous membrane of the middle ear or tympanum, and covers also the handle of the malleus just referred to. The middle layer or basis of the membrane consists of many fibres of connective tissue radiating from the handle of the malleus, and some circular ones forming a thickened margin at the circumference, where it is attached to the bone. Between the depressed part of the funnel and its margin the membrane is somewhat convex outwards. Blood-vessels, nerves and lymphatics are found especially in the skin and mucous membrane coverings of the membrane.

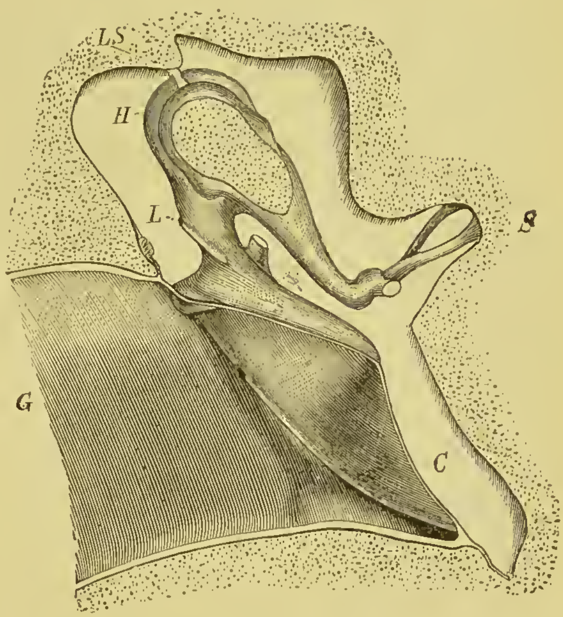

Fig. 357.—Tympanic Cavity and Ossicles of Left Side, seen from behind, magnified four times. The Section passes through the Incus.

G, External auditory meatus; *C*, cavity of the tympanum; *S*, stapes; *H*, malleus with *L* point of attachment of external ligament, and on opposite side attachment of tensor tympani muscle; *L.S.*, ligamentum superior.

The **middle ear** or **tympanum** is a cavity in the temporal

bone lying between the membrana tympani and the outer wall of the osseous labyrinth of the internal ear. It contains the *auditory ossicles* which stretch from the membrane to the *fenestra ovalis*, through which the sound waves are conducted to the perilymph of the labyrinth. It also contains ligaments and muscles connected with the ossicles, nerves and blood-vessels, while by the Eustachian tube it communicates with the cavity of the pharynx, so that an equal pressure of air is maintained on both sides of the membrana tympani. The ossicles of the ear are three in number, and form an articulated chain. The outer or malleus, attached by its handle to the membrana tympani, articulates by its head with the body of the middle bone in the chain—the incus; and the latter by its long process articulates with the head of the innermost of the three, the stapes, the base of which is fixed into and occludes the oval foramen, or fenestra ovalis. The cavity of the tympanum is lined by mucous membrane, continuous with that lining the Eustachian tube and the inner surface of the membrana tympani. The epithelium covering it is ciliated for the most part, but the ossicles and the membrana tympani are invested by a layer of flattened squames.

The *malleus* or *hammer* possesses a thickened upper portion or *head*, a *neck* or *cervix*, and a thinner lower portion, the *handle* or *manubrium*, which, directed forwards, downwards and inwards, is attached throughout its length to the membrana tympani. There are also two processes—a long slender one, the *processus gracilis*, passing to the Glasserian fissure, to the sides of which it is attached by ligamentous fibres (anterior ligament of the malleus); and a shorter process projecting from the handle beneath the cervix, attached to the upper part of the membrana tympani by the fibres of the external ligament of the malleus. The superior ligament connects the head of the malleus to the roof of the tympanic cavity. The *incus* or *anvil* possesses a body and two processes. The body presents a large articular facet for the head of the malleus, and this *inco-malleal joint* is somewhat peculiar, and will be referred to again when the action of the ossicles is considered. Of the two processes the shorter is connected by ligamentous fibres with the wall of the tympanum, while the longer lies parallel with the handle of the malleus, and articulates with the head of the stapes: the *stapes* or *stirrup* possesses a *head*, a *neck*, a *base*, and two *crura*. The head is directed outwards, and articulates with the long process of the incus; the base, covered on its vestibular side and edge with hyaline cartilage, is fitted into the fenestra ovalis, the margin of which is similarly covered,

and the cartilaginous surfaces are connected by elastic tissue which, however, permits of a certain amount of movement.

The muscles of the tympanum.—These are two in number, of which one is inserted into the malleus, and the other into the stapes. The *tensor tympani* arises from the cartilaginous end of the Eustachian tube and adjacent surface of the sphenoid bone, and passing through a bony canal towards the tympanic cavity, turns round the processus cochleariformis, almost at a right angle immediately in front of the fenestra ovalis. From this point it passes outwards, and is inserted into the handle of the malleus near its root. The tendon of the *stapedius* muscle issuing from the pyramid is inserted into the neck of the stapes. The tensor tympani is supplied by the fifth, and the stapedius by the seventh or facial nerve.

The *inner wall of the tympanum* presents some features of special interest. Near its upper part is the *fenestra ovalis*, closed normally by the base of the stapes and its annular ligament, but communicating, in the dried specimen, with the cavity of the vestibule. Below it is an elevation—the *promontory*—corresponding with the first turn of the cochlea. Below and behind this is the *fenestra rotunda*, closed by a thin membrane, sometimes called the *secondary membrane of the tympanum.* It separates the air of the tympanum from the perilymph of the scala tympani of the cochlea, and is composed of a middle fibrous basis covered on either side with the lining membrane of the adjacent cavity. It is concave towards the tympanum, and convex towards the inner ear. The *posterior wall of the tympanum* opens by the *antrum mastoideum* into numerous irregular cavities, the *mastoid cells*, which are lined by a membrane continuous with that of the tympanum generally. Below the orifice of the antrum is the projection known as the *pyramid,* the apex of which is pierced by the stapedius muscle.

Movements of the ossicles.—The handle of the malleus naturally follows the movements of the membrana tympani, to which it is closely attached, and when this membrane moves inwards the malleus and incus rotate as one bone round an axis passing backwards from the attachment of the malleus by its anterior ligament through the ligamentous attachment of the short process of the incus posteriorly. The student should make a point of realising this axis, as a proper understanding of the movements of the ossicles depends on it. Fig. 358 shows the ossicles of the left side seen from within, and it will be noted that though the bones have been described as external, middle and internal in position, the

malleus is also at the same time anterior to the incus. Fig. 359 demonstrates the axis of rotation from another point of view, and it will be observed that it is a horizontal section through the *right* tympanum. *A* is the body of the incus in section, *h* the head of the malleus, *lga* is the anterior ligament of the malleus, *ax* the axis of rotation.

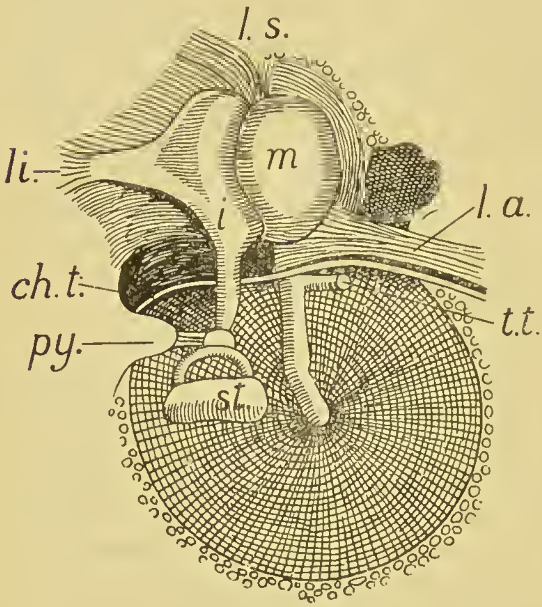

Fig. 358.—Left Membrana Tympani and Auditory Ossicles from the Inner Side and slightly from Above.

m, Malleus; *i*, incus; *st.*, stapes; *py.*, pyramid from which tendon of stapedius is emerging; *t.t.*, tensor tympani tendon cut; *l.a.*, anterior ligament of malleus; *l.s.*, superior ligament of malleus; *li.*, ligament of the incus; *ch.t.*, chorda tympani nerve.

As a consequence of the inward movement of the incus, the stapes articulating with its long process is also moved inwards, and as a result of the pressure it exerts on the perilymph of the vestibule, the secondary membrane of the fenestra rotunda is bulged or rendered convex to the tympanic cavity; the position being reversed when the membrana tympani resumes its previous position. That the membrane of the fenestra rotunda is thus affected is

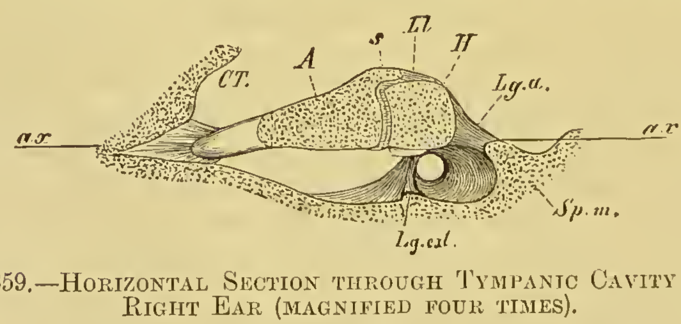

Fig. 359.—Horizontal Section through Tympanic Cavity of the Right Ear (magnified four times).

due to the fact that the inner ear is filled with lymph, and

that its walls are rigid except at this opening. That the incus follows the movements of the malleus thus closely when the membrana tympani is pressed inwards is due to the construction of the *inco-malleal joint*, already referred to. The lower margin of the articular surface of the incus exhibits a well-marked projection or tooth, which catches against or *interlocks* with the margin of the articular surface of the malleus. But if the handle of the malleus be drawn outwards by a reverse movement of the membrana tympani the bones cease to lock together as one, and the head of the malleus moves on the articular surface of the incus as in an ordinary joint. In this way is avoided the dragging of the stapes from the fenestra ovalis which might otherwise follow increased tension of the air in the tympanum.

The incus and malleus thus act as a crank lever and transmit the vibrations of the membrana tympani to the stapes and fenestra ovalis; but it must be noted that as the process of the incus is only about two-thirds of the length of the handle of the malleus, there is a diminution in the amplitude of the movements and a corresponding increase in their strength.

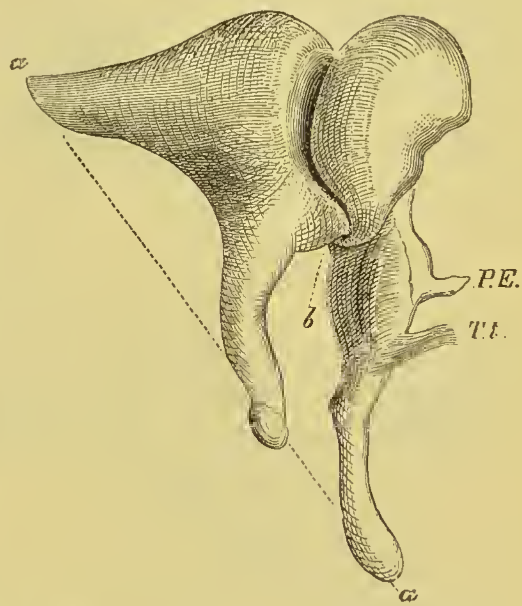

Fig. 360.—Malleus and Incus, showing the interlocking of the Inco-malleal Joint.

P.E., Processus gracilis; *T.t.*, tensor tympani attachment; *b*, tooth of incus interlocking with tooth of malleus; *a*, *a*, passes through the two ends of the crank lever formed by malleus and incus.

The tensor tympani muscle draws the malleus inwards as a whole, and with it the membrana tympani, which is thus rendered more tense. It is probably called into play in the perception of faint sounds, mechanically locking the inco-malleal joint and thus preventing escape of any of the vibrations. When the nerve supply is paralysed hearing is impaired, especially for faint sounds. The stapedius draws the head of the stapes backwards, pressing the hinder end of the base inwards and the anterior end outwards, the annular ligament being thus rendered tense and the bone steadied. It has been suggested

that its function is to damp the movements of the stapes when sounds are too loud, and in support of this theory it is found that in cases of paralysis of its nerve supply there is increased sensitiveness to loud sounds (Fig. 361).

The **internal ear** is developed from the *otic vesicle*, which is derived directly from the epiblast, and is not, therefore, like the optic cup, to be regarded as an outlying portion of the brain. The otic sac, lined by a layer of cubical cells, is met by divisions of the auditory nerve projected from the brain, and at the points of contact the lining epithelium undergoes special differentiation and comes into direct relation with the nerve-fibres. The otic sac does not, however, like the optic vesicle, undergo invagination to form a cup, but the cavity persists throughout life and is occupied by the *endolymph*. It is to be noted, also, that, as compared with the eye, a much smaller portion of the vesicle (only the special areas where the branches of the auditory nerve come into relation with the epithelium) is concerned with special sense.

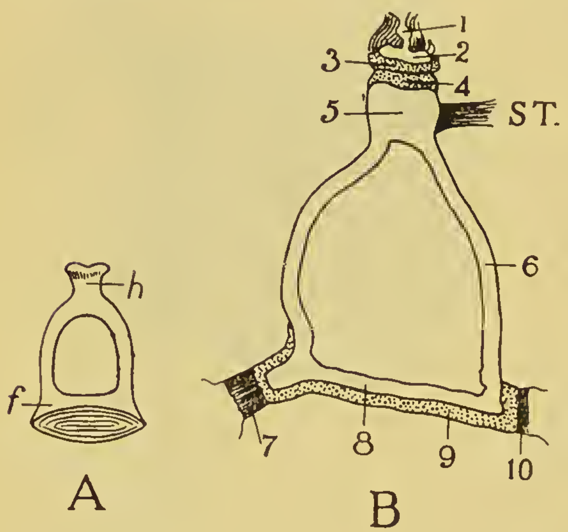

Fig. 361.—*A*, The Stapes (magnified four times). *h*, Head and neck; *f*, foot-plate.

B, Stapes in Situ (more highly magnified).

1, End of shaft of incus; 2, expansion or os orbiculare of same; 3, cartilage of same; 4, cartilage of capitulum of stapes; 5, capitulum of stapes; 6, hoop of stapes; 7, 10, membrane of fenestra ovalis; 8, foot-plate of stapes; 9, cartilage of foot-plate; *ST.*, insertion of stapedius muscle.

As the vesicle develops, its general form alters, so that it is no longer a simple sac, but a series of canals and cavities which, however, still communicate with each other. Changes also take place in the mesoblast around it, thus, the tissue immediately outside it constitutes a fibrous investment for the epithclial structures it encloses and the two together form what is known as the *membranous labyrinth*. Further out the mesoblast undergoes ossification, and the inner condensed shell of this bone whcn

dissected from the rest corresponds roughly to the membranous sac it encloses and is called the *osseous labyrinth*. It does not follow it exactly, however, one division of the osseous labyrinth, the vestibule, enclosing two portions of the membranous labyrinth —the utricle and saccule. The two labyrinths are in most places separated from each other by a well-marked lymph space containing the *perilymph*, but this space is sometimes absent from the fusion of the fibrous tissue of the membranous with the periosteum of the osseous labyrinth; or a bridle of connective tissue may extend between the two; or a branch of the auditory nerve on its way to the epithelial lining may connect them. The space containing the perilymph is lined by cells with a sinuous outline and is continuous with the lymph-spaces in the connective tissue bounding it.

We may now consider the disposition of parts in the internal ear a little more in detail.

The Membranous Labyrinth.

The membranous labyrinth consists of (1) the utricle and semicircular canals; (2) the saccule; and (3) the canalis cochlearis. The

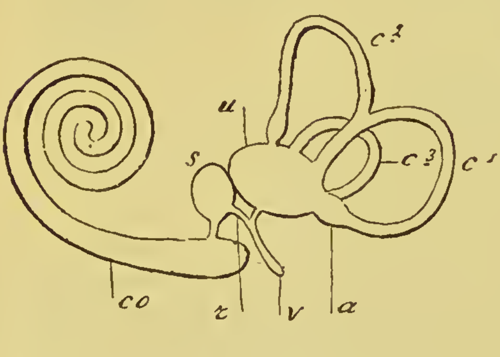

Fig. 362.—Membranous Labyrinth.

c^1, c^2, c^3, Semi-circular canals, note the ampullæ (*a*) where they join the utricle; *u*, utricle; *v*, ductus or sacculus endolymphaticus; *s*, saccule; *cr*, canalis reuniens; *co*, canalis cochlearis or scala media.

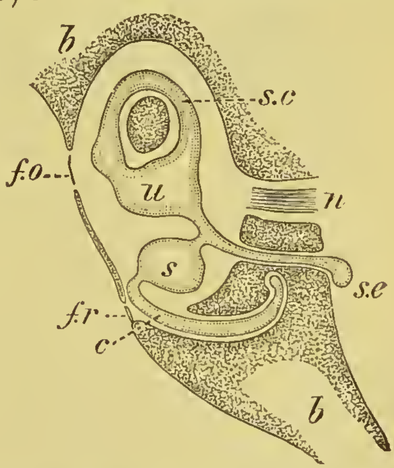

Fig. 363.—Diagrammatic representation of Internal Ear.

b, Bone; *s.c.*, semi-circular canal; *u*, utricle; *s*, saccule; *c*, cochlea; *f.o.*, foramen rotunda; *n*, auditory nerve; *s.e.*, saccus endolymphaticus.

utricle is an oval sac into which the semi-circular canals open at each end. Each semi-circular canal has thus two openings into the

utricle, and at one of these it exhibits an enlargement, called the ampulla. The utricle is in communication by the *ductus endolymphaticus* with the *saccule*, a smaller rounded portion of the labyrinth. The saccule is connected by the *canalis reuniens* with the *canalis cochlearis*, which is twisted into the form of a spiral and terminates blindly.

The relation of the membranous to the osseous labyrinth, as described above, is found more especially in the vestibule and semi-circular canals. The cochlear part of the membrane, which is the part concerned with the reception of auditory impressions, differs from the rest in its disposition, its relation to the osseous labyrinth, and the distribution of its nervous supply. To begin with it is coiled as a spiral of two-and-a-half turns round a central osseous stem or *modiolus*, and this gives to the osseous labyrinth in this part the appearance of a snail's shell, and hence the name *cochlea*. In a vertical section the cavity of the bony canal may

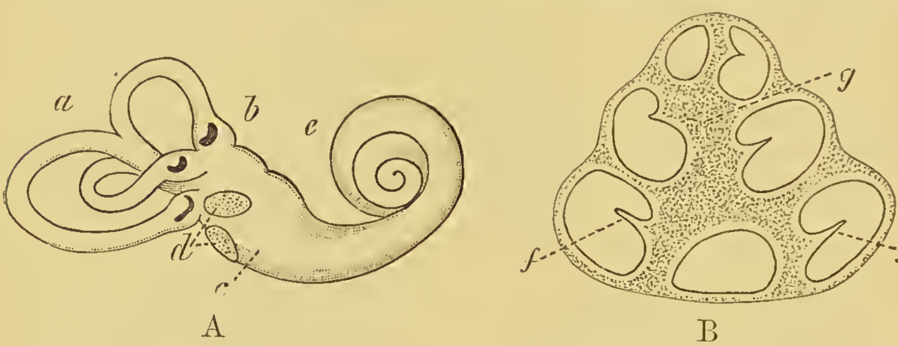

Fig. 364.—(A) Bony Labyrinth dissected out from rest of Temporal Bone. (B) Bony Cochlea in Vertical Section.

a, Semi-circular canals; *b*, ampullæ; *c*, vestibule; *d*, macula and crista; *e*, cochlea; *f*, osseous spiral lamina; *g*, modiolus.

be cut five times transversely, and will present somewhat the appearance shown in Fig. 364, B. It will be seen that the bony canal is partially divided into two secondary ones by a projection outwards from the central stem or modiolus, called the *osseous spiral lamina*. The canalis cochlearis, triangular in shape in section, is so placed that the base of the triangle is applied to the outer wall of the bony canal, while the apex joins the edge of the spiral osseous lamina; and this definite relation of the parts is retained throughout the spiral. It follows from this that at the outer* side of the canalis cochlearis the peri-

* "Outer" here refers to its relation to the modiolus.

lymph space is entirely absent, the two labyrinths, osseous and membranous, being adherent in this region; but above and below the lymph-space extends throughout its length. The lymph-space is thus divided into two by the osseous spiral lamina and the canalis cochlearis, and these two divisions of it have received different names. The one above the canalis, inasmuch as it communicates at the base of the cochlea with the perilymph space of the vestibule, is termed the *scala vestibuli*; while that below, which terminates at the base of the cochlea at the fenestra rotunda which separates it from the tympanum, is called the *scala tympani* (see Fig. 365).

We have yet to inquire what becomes of the two scalæ as they are followed to the apex of the cochlea. It has already

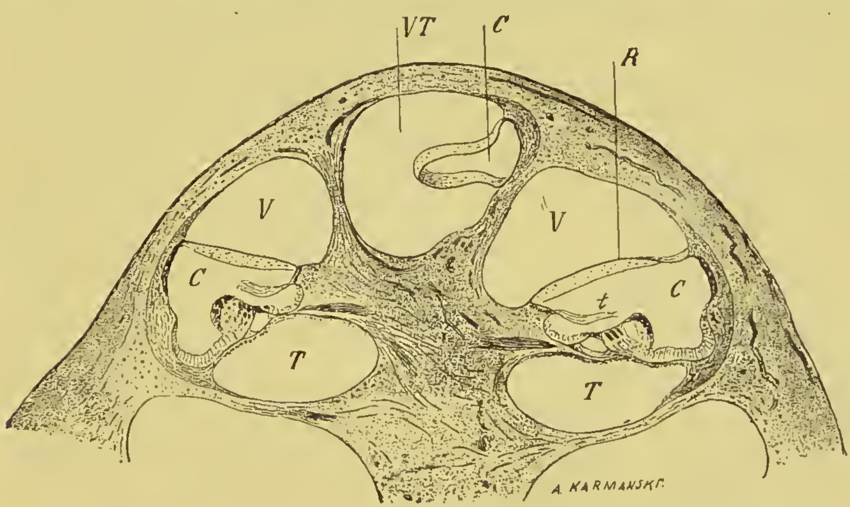

Fig. 365.—Vertical Section of Cochlea of Guinea-pig.

V, Scala vestibuli; *T*, scala tympani; *VT*, where the two meet; *C*, scala media; *R*, Reissner's membrane; *t*, membrana tectoria.

been stated that at this point the canalis cochlearis terminates blindly. The osseous spiral lamina also ends in the form of a hook, the *hamulus*, and thus the two scalæ, with nothing further to separate them, join each other here through a small opening, the *helicotrema*. When the stapes is pressed into the foramen ovale, the wave started in the lymph of the vestibule of the osseous labyrinth travels along the scala vestibuli, passes through the helicotrema, descends the scala tympani, and impinges on the membrane of the fenestra rotunda.

The distribution of the cochlear nerve is also peculiar. The auditory nerve divides into two main divisions, the *cochlear*

and *vestibular.* Of these the latter divides again into five smaller branches, of which three pass to the ampullæ of the semi-circular canals and terminate in localised swellings in the membranous labyrinth, the *cristæ acusticæ;* one passes to the utricle and one to the saccule, and each terminates in an oval swelling, the *macula acustica.* Thus the area of distribution of each of these five branches is strictly limited to one part of the epithelial lining. But in the cochlea the nerve is distributed along the whole length of one side of the canalis cochlearis from the base to the apex of the spiral, and the modified epithelium along this side is termed the "organ of Corti."

Structure of the maculæ and cristæ acusticæ.—The utricle, saccule and semi-circular canals are lined by polygonal, flattened, nucleated cells, resting on a tunica propria formed of a hyaline surface condensation of the surrounding vascular fibrous membrane. Outside this is the perilymph, as already stated, the space containing it being broken by bridles of connective tissue, uniting the membranous labyrinth to the periosteum of the bone. The perilymph space is lined with sinuous epithelium and communicates with the subdural lymph-space of the auditory nerve.

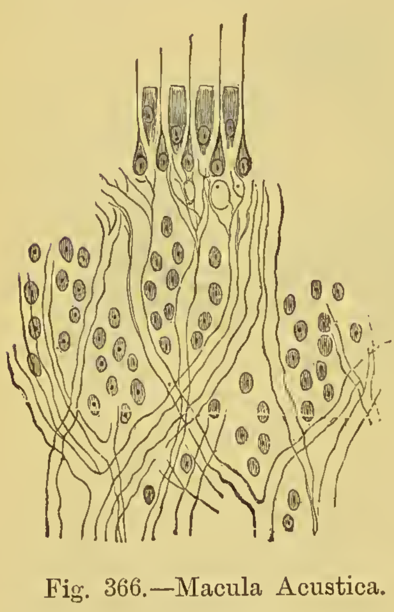

Fig. 366.—Macula Acustica.

The macula of either utricle or saccule consists of an oval thickening of the membranous wall—a thickening involving both the epithelium and the connective tissue outside it. The thickened epithelium contains hair-cells and sustentacular cells, the latter corresponding with the fibres of Müller in the retina and the cells of Deiters in the organ of Corti. The hair-cells are the most superficial and are columnar in shape. They extend to about the junction of the inner and middle thirds of the layer or a little more, where they terminate in a rounded base containing the nucleus. The free end of one of these cells possesses a bayonet-like "hair" or process projecting into the cavity of the sac, apparently composed of a number of finer hairs stuck together, much as those of a wet paint-brush are. The supporting cells are

somewhat rod-like, and extend from the surface of the epithelium, where they join a cuticular membrane which encloses the ends of the hair-cells, to the tunica propria beneath. These rods at some part of their course outside or beneath the hair cells exhibit an oval nucleus, the nuclei giving rise collectively to the appearance of a nuclear layer outside the layer of hair-cells. At the edge of the macula the differentiated epithelium just described changes to a layer of tall columnar cells which join the flattened polygonal cells lining the cavity generally, as the level of the sac wall is reached.

The nerve to the macula spreads out in a fan-like manner as it passes through the connective tissue thickening to the epithelium, and the fibres lose their grey and medullary sheaths as they pass through the tunica propria. In the epithelial layer the naked branching axis-cylinders pass between the supporting cells, and each terminates as a brush of nerve-fibrils which surround the base of a hair-cell. There is thus apparently no direct anatomical continuity between the hair-cells and the nerve-fibres.

Above the hair-cells, and supported by the hairs which come in contact with it, is a structureless mucinous membrane, containing rhombic or octahedral crystals of calcium carbonate, which is sometimes termed the *otolith*.

The cristæ acusticæ of the semi-circular canals have the same structure as the maculæ of the utricle and saccule, but the swelling is in the form of a ridge or crest; there is no otolith and the hairs of the cells are longer.

Structure of the organ of Corti.—The edge of the osseous spiral lamina projecting from the modiolus is thin, but the connective tissue covering it is thickened on its upper surface to form the *limbus laminæ spiralis*. Externally this is hollowed out or grooved and presents two lips, the upper of which is termed the *labium vestibulare*, and the lower the *labium tympanium*, the hollow between them being the *sulcus spiralis*. We have used the words upper and lower, as for purposes of description it is more convenient to suppose the apex of the cochlea to be above and the base below, but it must be borne in mind that this is not its natural position *in situ*.

The upper lip of the limbus—the labium vestibulare—is split at its edge radially into a series of *auditory teeth*, which resemble somewhat the keys of a piano when looked at from above. Cells are absent from this part of the connective tissue, which exhibits a strong, apparently homogeneous matrix. From the upper surface of the vestibular part of the limbus, or *crista spiralis*, the *membrana tectoria* projects outwards over the organ of Corti.

The superior wall of the canalis cochlearis, when traced from the upper surface of the limbus, passes outwards and upwards as the *membrane of Reissner* till it reaches the periosteum of the outer wall of the bony canal, with which its fibrous basis becomes continuous, the epithelium on its under surface being continued over the periosteum, and here forming the base or outer side of the triangular canal. The membrane of Reissner has much the same structure as the rest of the wall of the membranous sac where it is not specially differentiated. The epithelium on its lower or inner side is flattened, and the cells are polygonal in outline. Above this, or external to it, is a median basis of delicately-fibrillated or homogeneous tissue, continuous with that of the limbus on the one hand, and the periosteum of the bony canal on the other. Beyond this is a layer of sinuous epithelial cells, similar to those lining the rest of the scala vestibuli.

If the flattened polygonal cells of the inner surface of the membrane of Reissner be traced on to the limbus, they are found to be reflected over its upper surface, but become cubical in shape where they sink between the auditory teeth. Traced further in the same direction they join a layer of cubical or columnar cells lining the sulcus spiralis, and these in turn pass into the epithelium of the organ of Corti.

The periosteum of the external wall of the cochlea, where it bounds the base of the cochlear triangle, is considerably thickened, and the thickness is seen to increase as it is traced downwards from the point where the epithelium of Reissner's membrane is reflected upon it. It is thickest of all where the epithelium leaves it again to pass inwards upon the *membrana basilaris;* decreasing again as it is followed downwards from this point along the wall of the scala tympani. At its thickest part the fibres of the periosteum converge to a point (in section) to meet the membrana basilaris, and this projecting line is termed the *spiral ligament.* The epithelium reflected from the under surface of Reissner's membrane is tall and columnar in character where it forms the outer wall of the canalis cochlearis resting on the thickened periosteum above the spiral ligament. Capillary vessels penetrate between these cells, and the line formed by them, as seen from the canal, is termed the *stria vascularis.*

The *basilar membrane* stretching between the lower lip of the limbus and the spiral ligament represents the fibrous layer of the wall of the canalis cochlearis in this region, and consists of a number of fibres running radially in a homogeneous matrix. The fibres chemically resemble elastic tissue, and in the human cochlea there may be as many as 24,000 of them.

They vary considerably in length as the membrane increases in breadth from the base of the cochlea upwards, while the breadth of the osseous spiral lamina diminishes. The lower, outer, or tympanic surface of the membrane is covered by a layer of sinuous cells, similar to those lining the scala tympani generally; and between the epithelium and the fibrous basis of the membrane, beneath the tunnel of Corti, is found a spirally running vessel, the *vas spirale.* The epithelium lining the upper or inner surface of the basilar membrane is continuous on the one hand with the cells lining the sulcus spiralis of the limbus, and on the other with those covering the stria vascularis of the outer cochlear wall. A portion of this epithelium is specially developed into the organ of Corti.

The **organ of Corti.**—As the epithelium is traced outwards from the sulcus the cells become more columnar in shape, until they reach a considerable height, while the outermost of them (in section) is specially differentiated. Its lower extremity, like that of the cylinder or hair-cells of the maculæ, contains the nucleus and is rounded, and reaches only half-way down through the depth of the epithelium as a whole. Beneath its rounded end other nuclei are seen (those of supporting cells), which extend from the connective tissue of the osseous spiral lamina below to the surface of the epithelium, where they join a cuticular formation. The superior extremity of the cylinder cell exhibits a hyaline border bearing ten or fifteen short stiff hairs arranged in a curve, as shown in Fig. 367.

Immediately outside this *inner hair-cell*, as it is called, are the *rods* or *pillars of Corti.* These are two in number, *i.e.*, in a vertical transverse section of the tunnel, but in reality there are some 10,000 or more. Each rod possesses a *head* with a process extending from it externally, a *body* or *limb*, and an expanded *foot* cemented to the membrana basilaris. They slope towards each other from below upwards, so that the head of the external rod rests on a corresponding depression in the head of the inner. The somewhat triangular space between the limbs and the basilar membrane is the *tunnel of Corti*, winding spirally upwards from the base to the apex of the cochlea with the rest of the *membranous spiral lamina*, which includes the basilar membrane and the structures upon it. The rods are developed as a cuticular formation from "basilar" cells, the nuclei of which are in evidence on the tunnel side of each foot, and the protoplasm of the cells themselves—one to each rod—may often be seen extending along the limbs of the pillars and thus lining them on the inside. The

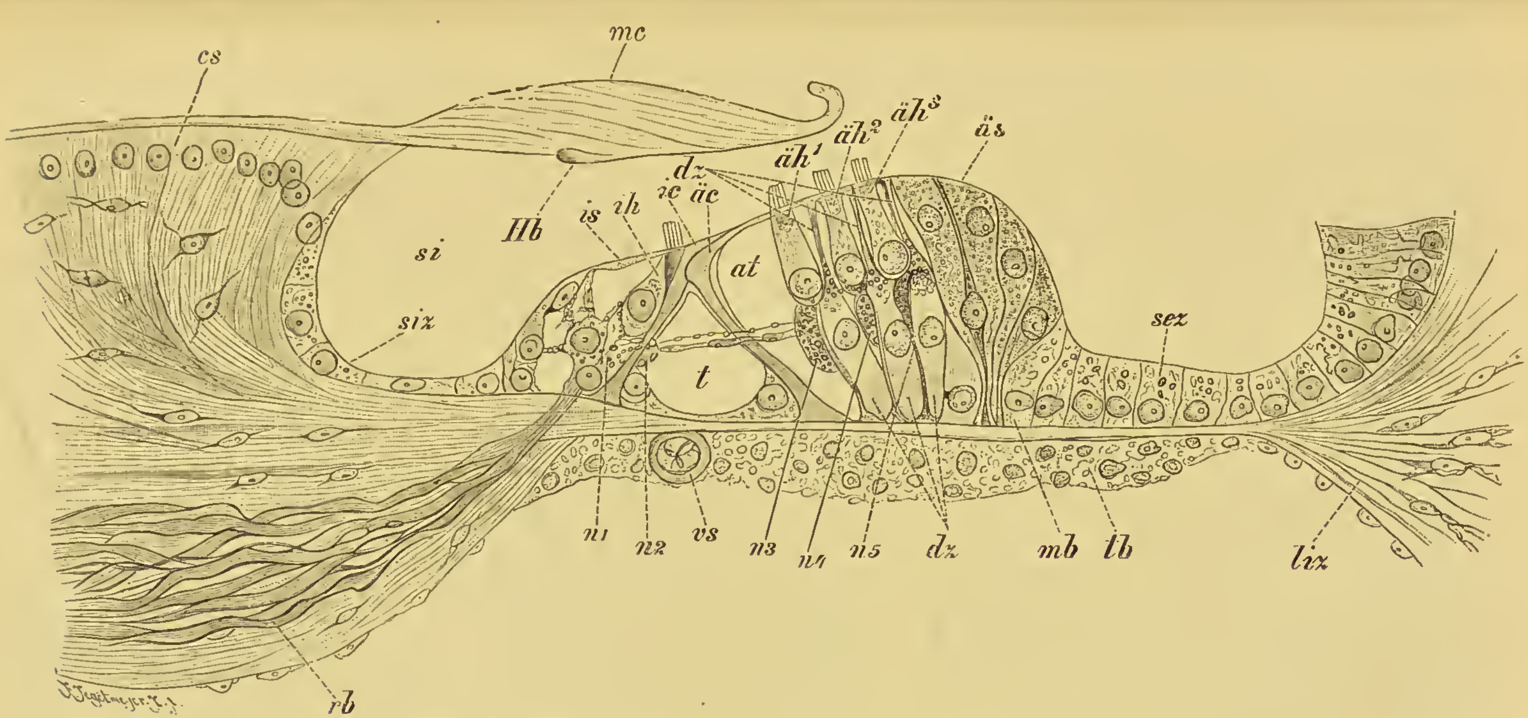

Fig. 367.—Section of Organ of Corti of Man (highly magnified).

cs, Crista spiralis; *mc*, membrana tectoria; *rb*, nerve-fibres passing to organ of Corti; *siz*, epithelium of sulcus spiralis, *si*; *mb*, membrana basilaris (the line is carried a little too far); *liz*, ligamentum spirale; *tb*, epithelium of tympanic side of basilar membrane; *vs*, vas spirale; *n*1, inner spiral strand of nerve-fibrils; *n*2, spiral strand of tunnel; *n*3, *n*4, *n*5, outer spiral strands; *is*, inner supporting cells; *ih*, inner hair-cell; *ic*, inner pillar of Corti; *äc*, outer pillar of Corti; *t*, tunnel of Corti; *äh*1, *äh*2, *äh*3, outer hair-cells; *dz*, Deiters' cells; *äs*, Hensen's supporting cells; *sez*, cells of Claudius; *si*, sulcus spiralis.

external processes from the heads of the rods are continuous with the *membrana reticularis*, also of cuticular origin, which gives support to the ends of the outer hair-cells. The tunnel of Corti, however, is not complete, for the limbs of the rods are of less diameter than the heads and feet, and through the spaces between them the filaments of the cochlear nerve reach the outer hair-cells.

On the outer side of the rods of Corti there are in the human subject four rows of outer hair-cells, though this number may be exceeded in the upper turns of the cochlea, and reduced to three in the lowermost turn. In many animals only three rows of cells are found. Beyond the hair-cells the epithelium is composed of very tall columnar cells, the *cells of Hensen*, forming the highest part of the organ. These pass with some suddenness into the single layer of cubical *cells of Claudius* which rest on the basilar membrane and are in turn continued into the cells covering the stria vascularis. The *outer hair-cells* resemble the inner, ending about the middle or outer third of the epithelial development in a rounded extremity containing the nucleus, and bearing at their upper end a number of hair-like processes projecting from a hyaline border. The upper end of each cell is surrounded by one of the rings of the cuticular membrana reticularis. In addition to the hair-cells, there are supporting cells, or *cells of Deiters*, each one of which lies to the outer side of the corresponding hair-cell and has a definite relation to it. They are elongated in form and extend from the basilar membrane below to the phalanx of the reticular membrane immediately external to the ring of the hair-cell to which they belong. About its middle, or a little above, the lower end of the hair-cell abuts against, and is probably cemented to it; and below this point the sustentacular cell thickens to allow for its nucleus. A cuticular band runs along the inner side of each cell, and doubtless bears the same relation to it that the rods of Corti do to the basilar cells already mentioned.

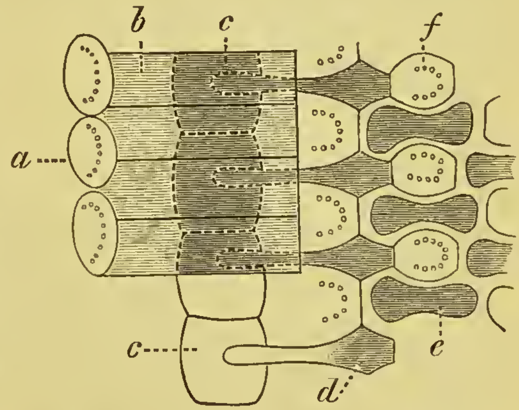

Fig. 368.—Surface View of Part of Organ of Corti (after Retzius).

a, Inner hair-cell; *b*, heads of inner rods; *c*, heads of outer rods with *d* phalangeal processes; *e*, phalanges; *f*, second row of outer hair-cells.

The *membrana reticularis*, the cuticular membrane to which

reference has been made, extends from the processes of the rods of Corti to the edge of Hensen's cells. It is not a continuous sheet, but is formed of rings or *annulæ*, separated from each other by *phalanges*, the rings surrounding the ends of the hair-cells, and the phalanges receiving the upper extremities of the cells of Deiters, which are attached to their under surface. Fig. 368 shows a surface view of part of the organ of Corti.

The *membrana tectoria*, also cuticular in its origin, is attached to the upper surface of the limbus from the angle formed by the membrane of Reissner, and stretching over the organ of Corti is perhaps united at its margin to the edge of Hensen's cells. In preparations, however, the free margin is found unattached and rolled up somewhat like a scroll, possibly due to injury. It is composed of a soft elastic substance finely striated radially, and, as may be seen in the figure, is thickest in its middle part. It is applied to the surface of Corti's organ much as the otolith is to the maculæ of the utricle and saccule, and may act as a damping mechanism.

The *cochlear nerve* occupies a central canal in the axis of the modiolus, and here gives off a spiral lamina of nerve-fibres, which traverses the osseous spiral lamina to the organ of Corti. On the spiral lamina, at about the junction of the osseous lamina with the modiolus, is found a round or oval (in section) collection of nerve-cells, the *spiral ganglion*, which is contained in the *spiral canal.* The cells are bipolar, each process possessing a medullary sheath. The fibres passing from the ganglion leave the tympanic lip by foramina beneath the inner hair-cells, and as they emerge from the connective tissue they lose their medullary sheath, and continue as naked axis-cylinders. Some of the strands of fibrillæ into which these split assume a spiral direction beneath the inner hair-cells and form the *inner spiral strand*, and from it a network of fibrils passes up to invest the lower ends of the inner hair-cells. Other strands pass on to the tunnel between the limbs of the inner rods, and one of these strands turns and becomes the *spiral strand of the tunnel.* The others pass between the outer rods and form four *outer spiral strands* beneath the outer hair-cells, and from these strands a network of filaments arises to invest the bases of the outer hair-cells. There are thus six strands in all.

Functions of the membrana tympani and auditory ossicles.— The aerial vibrations are received by the tympanic membrane and transmitted through the chain of auditory ossicles to the perilymph of the labyrinth. But whereas such a membrane as a drum-head

possesses a note of its own, *i.e.*, will vibrate in response to some particular note rather than to others, the tympanic membrane receives and responds to practically all vibrations. This may be explained by the fact that it is not evenly stretched but is funnel-shaped, nor is it normally tightly stretched. If, however, the pressure of the air in the tympanic cavity be increased or diminished so that the tension of the membrane is increased, the sense of hearing is impaired. The function of the Eustachian tube, by which the cavity of the middle ear communicates with the throat, is the maintenance of an even pressure, *i.e.*, that of the atmosphere on each side of the tympanic membrane. If the Eustachian tube be occluded by a swelling of its mucous membrane, the pressure on the inside of the membrane is lessened, the membrana tympani drawn inwards, and deafness results. The pressure is diminished in the tympanic cavity because the blood-vessels of its walls give out less CO_2 than the oxygen they absorb and the difference is not rectified by communication with the external air. Again, if the nostrils be held between the finger and thumb and the mouth closed, and a forcible expiration made into the nose, air is forced along the Eustachian tube into the tympanum, the membrana tympani is forced outwards and impairment of hearing results, but readily disappears if the pressure be again equalised by releasing the nostrils. In other words, it is only when the pressure of the air is the same inside and outside the tympanum that the normal vibration of the membrana tympani is possible. The Eustachian tube is generally closed by apposition of the surfaces of the mucous membrane lining it, but it is opened by the tensor palati muscle during the act of swallowing.

From the membrana tympani the vibrations are transmitted by the auditory ossicles, which vibrate *en masse*, to the perilymph through the fenestra ovalis, and reach the endolymph of the canalis cochlearis through Reissner's membrane, and so affect the hair-cells of the organ of Corti. But though normally the sound waves pass along the auditory ossicles, they may be conducted to the endolymph through the other osseous structures of the skull. Thus a tuning-fork or watch held between the teeth or placed on the top of the head is heard even though the ears are stopped; in fact it is heard better when the ears are stopped, as sound is thus prevented from passing out of the ear from the vibrating membrana tympani.

Auditory perceptions.—A musical *note* or *tone* is distinguished from a *noise* by the periodicity of the movements of the vibrating elastic body giving rise to it, *e.g.*, the vibrating string or membrane

executes the same movements in equal intervals of time. On the other hand, a noise is caused by the non-periodic movements of the vibrating body, as when it executes equal movements in unequal intervals of time. The difference between a noise and a musical note may be readily demonstrated by means of the *syren*. If a rotatory disc be perforated with forty holes at an equal distance from each other, and the disc be rotated while a current of air is directed against it, the air will be rarefied and condensed exactly forty times in each revolution; and inasmuch as the condensations (and rarefactions) are separated from each other by equal intervals, the note or tone yielded is found to be a musical one. If, however, we take a disc with the holes perforated at unequal distances from each other, only a whirring noise results when it is made to revolve and a current of air directed against it, because the movements of the vibrating body, *i.e.*, the condensations and rarefactions of the air, are non-periodic.

In a musical tone the ear appreciates intensity, pitch and quality (see "Voice and Speech").

Perception of pitch and quality of compound tones.—When a mixture of rays of light of different wave-length falls on the retina the sensation produced is, as we have seen, a simple one, *i.e.*, we do not recognise its component parts. But the ear is capable of analysing the compound sensation when aerial vibrations of different frequency fall on the membrana tympani. The physical resultant of all the tones strikes the membrane as a single wave and therefore analysis of the compound vibrations into their constituents must take place in the inner ear or brain. According to the theory of Helmholtz, analysis of pitch takes place in the labyrinth. If we sing a note in front of the open piano, the strings attuned to that particular note vibrate sympathetically, the rest being unaffected, and Helmholtz supposed that an analogous system of resonators might be found in the organ of Corti by which the complicated wave forms of musical tones were resolved into their components. "If we could so connect every string of a piano with a nerve-fibre that the nerve-fibre would be excited and perceived as often as the string vibrated, then, as is actually the case in the ear, every musical note which affected the instrument would excite a series of sensations exactly corresponding to the pendulum-like vibrations into which the original movements of the air can be resolved, and thus the existence of each individual over-tone would be exactly perceived, as is actually the case with the ear. The

perception of tones of different pitch would, under these circumstances, depend upon different nerve-fibres, and hence would occur quite independently of each other. Microscopic investigation shows that there are somewhat similar structures in the ear" (Helmholtz). Helmholtz at first supposed the rods of Corti to be the vibrating structures, the movement being transmitted to the nerve-fibres directly, or through the hair-cells. But birds have no rods of Corti, and he next selected as resonators the fibres of the basilar membrane, which, as we have seen, increases in breadth from below upwards, the idea being that there would be a fibre of this stretched membrane to correspond to every possible simple tone. We may term Helmholtz's the *theory of peripheral analysis of pitch.*

Another view, that of Rutherford and Waller, assigns the analysis to the brain, and is known as the "telephone theory." We may suppose that the basilar membrane vibrates as a whole to all sounds, the hair-cells are similarly affected, and nerve impulses pass from them to the brain, where they are analysed. In fact, the basilar membrane is "the internal drum-head, repeating the complex vibrations of the membrana tympani and vibrating in its entire area to all sounds, although more in some parts than in others, giving what we may designate as acoustic pressure patterns between the membrana tectoria and the subjacent field of hair-cells. In place of an analysis by sympathetic vibration of particular radial fibres, it may be imagined that varying combinations of sound give varying pressure patterns, comparable to the varying retinal images of external objects" (Waller). This is the *theory of central analysis of pitch.*

Though a considerable amount of evidence can be adduced in support of both theories, there seems on the whole to be more in favour of the original peripheral one of Helmholtz. In the first place the extreme complexity in structure of Corti's organ, and the remarkable variation in the characters and size of its various elements—such as the supporting and hair cells and in the length of the fibres in the basilar membrane—would point to a more specialised function of the parts than that of a mere transmitter of sound, such as a telephone plate.

Secondly, Baginsky has demonstrated that destroyal of the upper whorls of the cochlea is followed by the loss of perception of low tones, and there is a certain amount of clinical evidence which would incline us to the same belief, viz., that definite portions of the cochlea are concerned in the reception and analysis of definite tones.

Hering has also shown that in the arthropoda certain hairs

will only vibrate fully in response to musical tones of definite pitch.

One of the chief objections to the theory was the belief that there was an insufficiency of terminals in the cochlea to respond to the vast number of tones perceptible to the musical ear; M'Kendrick has demonstrated, however, that this is probably incorrect, and that the terminals are sufficient in number to respond to tones varying only the one-thirtieth of a tone from one another.

The question is, however, of too complex a nature to be studied further here.

The rest of the labyrinth containing the maculæ and cristæ acusticæ of the utricle, saccule, and semi-circular canals is concerned not with hearing, but with equilibration, and will be considered in the section dealing with cerebellar function (page 748 *et seq.*).

The Senses of Smell and Taste.

The **sense of smell**.—The **olfactory membrane** covers the upper turbinated and part of the middle turbinated bone, and the upper third of the septum nasi. It has been shown, however, that probably only a very small part of this membrane is actively concerned in smell. Von Brunn holds that it is only about 1 cm. across and that it is situated on the superior turbinate and the opposing surface of the septum. It is thicker than the respiratory membrane lining the nasal cavity below, and is of yellow colour in man, from the presence of pigment. The epithelium exhibits two kinds of cells—a row of cylinder-cells placed palisade-wise at the surface, with a well-marked nuclear layer beneath it, the whole resting on a layer of connective tissue, through which

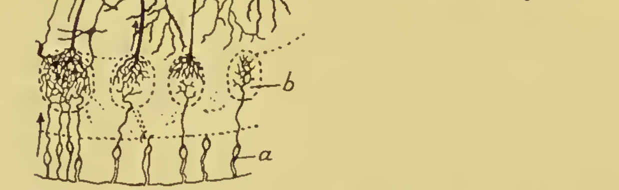

Fig. 369.—Diagram of the Olfactory Apparatus (after Cajal).

a, Olfactory cells, with their peripheral and central processes; *b*, olfactory glomeruli; *c*, mitral cells; *d*, axons of mitral cells passing backwards to the cerebrum; *e*, olfactory region in the cerebrum.

pass the non-medullated fibres of the olfactory nerve. The *cylinder-cells* are continuous with the ciliated cells of the respiratory membrane; and the free extremity of one of them reaches the surface, of which it forms a part, while the lower end contains an oval nucleus, and is prolonged into irregular processes, which become lost between the nuclei of the nuclear layer. The second variety of cell, the *rod-cells* of the nuclear layer, are the olfactory cells proper (Fig. 369), and each contains a spherical nucleus, surrounded by a little protoplasm, which is prolonged as a rod-shaped process to the surface, and projects a little beyond it. The central process, often beaded, passes down between the more deeply placed nuclei of the layer and becomes connected with one of the terminal branchings of the olfactory nerve. *Basal cells* next to the dermis are also described. They are small, conical in shape, and possess an oval nucleus. The cylinder cells contain granules of yellowish-brown pigment.

In the frog the rod-cells bear at their free extremity a brush of fine hair-like processes, but these are absent in man.

The olfactory membrane possesses a number of glands, the alveoli of which lie in the sub-epithelial connective tissue, their ducts opening on the surface. They are of the tubular variety, and simple, or with one or two branches. The cells lining them are columnar and serous in character, and contain a yellowish-brown pigment. These are *Bowman's glands.*

Olfactory sensations are produced by the action of gaseous substances or very finely divided solid particles upon the bipolar cells of the olfactory membrane, the gas or air suspending the solid particles being brought in contact with it during the act of breathing. The sense of smell is also excited when vapours are drawn into the mouth and expired through the posterior nares, as when tobacco smoke is expelled through the nose. In this instance, however, in addition to the stimulation of the olfactory nerve terminations, the terminal filaments of the nasal branch of the fifth—the nerve of common sensation for the nose—are also stimulated; and this happens when any pungent vapour, such as that of acetic acid, is inhaled. When the olfactory nerve is paralysed, and the sense of smell lost, substances such as acetic acid and ammonia still affect the terminal branches of the fifth nerve, but this must be distinguished from true olfactory sensation.

Aromatic substances of a non-irritant character, dissolved in salt solution, may still excite the sensation of smell, but if the mucous membrane of the nose be at all damaged the odour is no longer perceived.

When the membrane is stimulated by electricity a sensation

similar to the smell of phosphorus is experienced at the kathode on closing, and at the anode on opening.

The sense of smell is extremely delicate, so little as $\frac{1}{1000000000}$ of a grain of musk being appreciable; and in such animals as possess a keener sense than man the extent of the olfactory region is correspondingly extended.

It is not possible at present to give a scientific classification of odorous substances, as we know so little of their *modus operandi:* we can only say that some are purely olfactory, such as simple scents or perfumes; others affect both the olfactory and ordinary sensory nerves of the nose, such as acetic acid; while yet other substances, such as carbonic acid, affect only the nerves of common sensation and have no true smell.

The sense of taste is closely associated with that of smell, and the two are often to a great extent complementary to each other, as when *flavour* is concerned. The flavour of a food, such as roast beef, is due to stimulation of both the olfactory and gustatory cells, and is consequently largely lost if one has a cold and the olfactory sense is in abeyance. Wines also stimulate both senses, and their "bouquet" is the result of olfactory stimulation. An instance of a similar correlation of three senses is afforded by tobacco smoking, in which the optic nerve also plays a part; the sensation being appreciably less if the act is carried out in the dark.

The **sense of taste.**—The tongue is invested with a layer of connective tissue from which septa pass into the organ between the various muscles of which it is composed; the whole being covered with a layer of stratified squamous epithelium, continuous

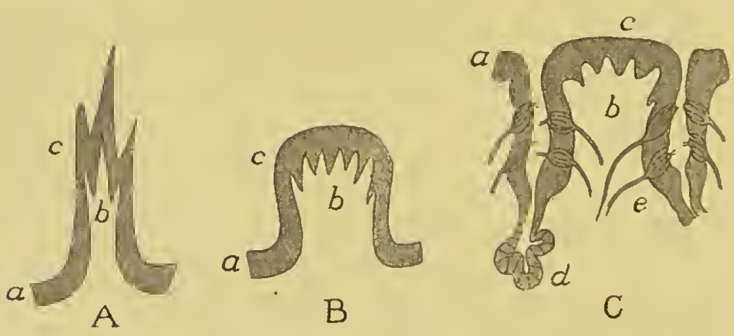

Fig. 370.—Diagrammatic representation of Papillæ of Tongue.

A, Filiform papillæ. B, Fungiform papillæ. C, Circumvallate papillæ. *a*, Epithelium lining mouth; *b*, fibrous tissue papilla, with secondary papillæ upon it; *c*, epithelium covering papillæ; *d*, serous gland (Ebner's) opening into vallum round circumvallate papilla.

with that of the cavity of the mouth generally. Over the whole of the superior surface of the tongue the epithelium is raised into papillæ containing a core of connective tissue; of these papillæ there are three varieties—*filiform*, *fungiform*, and *circumvallate.* The connective tissue core of each is divided into a series of secondary papillæ, which, in the case of the first-named, bear corresponding projections of epithelium. The three varieties are shown in the accompanying diagram (Fig. 370).

The filiform papillæ occur in greatest number and are found on the dorsum of the tongue except at the edges and tip; the fungiform are found at the tip and along the edges of the upper surface; while the circumvallate, eight to twelve in number, are arranged in the form of a V at the posterior part of the dorsum, the angle of the V being directed forwards. As their name indicates, they differ from the other two kinds in being surrounded by a *vallum* or ditch, along the sides of which taste-buds are found, and into the bottom of the ditch *Ebner's serous glands* open. When these glands secrete, the ditch is washed out from below upwards, and this prevents it becoming clogged, which it would otherwise do. The secretion also serves to dissolve sapid substances, and to bring them into contact with the sense-endings in the taste-buds.

Fig. 371.—Vertical Transverse Section of Papilla Foliata of Rabbit's Tongue.

p, Central lamina of folium; *p'*, lateral lamina of folium; *g*, taste-bud; *n*, sections of nerve-bundles; *a*, serous glands; *v*, vein.

Taste-buds, the terminal organs of the sense of taste, are found in the stratified epithelium of certain parts of the tongue and pharynx. As we have seen, they are found in the sides of the circumvallate papillæ and in the opposing wall of the vallum surrounding them. They are found in the epithelium of the fungiform papillæ, in that of the soft palate and neighbouring parts, and on the epiglottis. They are scattered in the general epithelium covering of the posterior third of the tongue, and are especially numerous in a small area in front of the anterior pillars of the fauces, corresponding probably to the *papilla foliata* of the rabbit. This is a small leaf-like portion of epithelium on each side of the tongue at its base, which is thrown into folds, the taste-buds being placed along the sides of the intervening furrows. Taste-buds are small oval collections of epithelial cells which have been differentiated from the epithelium of the mouth, generally to subserve a special function. They exhibit two kinds of cells—(1) *outer protective,* or *sustentacular cells,* which are fusiform, nucleated, and arranged much as the staves of a barrel around (2) the *gustatory cells.* These terminal sense-cells are narrower than the others and possess a nucleus and two processes. The peripheral process terminates in a *taste-hair* which projects through the open end of the barrel, which is termed the *gustatory pore.* The central process passes towards the base of the barrel, where it terminates, often after branching, in a free extremity. The fibres of the gustatory nerve lose their medullary sheath as they enter the base of the taste-bud, and run as branching axis-

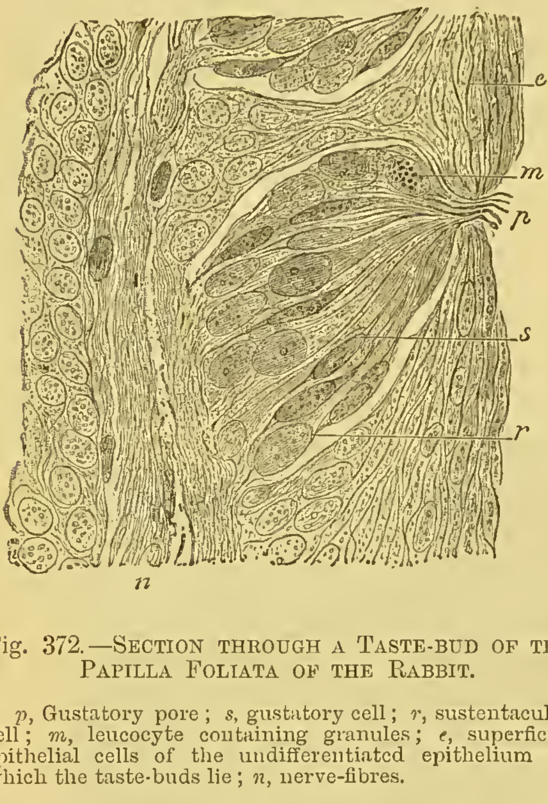

Fig. 372.—Section through a Taste-bud of the Papilla Foliata of the Rabbit.

p, Gustatory pore; *s*, gustatory cell; *r*, sustentacular cell; *m*, leucocyte containing granules; *e*, superficial epithelial cells of the undifferentiated epithelium in which the taste-buds lie; *n*, nerve-fibres.

cylinders among the gustatory cells (Fig. 372). According to Retzius they are not directly continuous with the cells by their central processes as was previously thought to be the case.

The regions of the mouth concerned in taste are not strictly defined, but may be taken to include roughly the root of the tongue in the neighbourhood of the circumvallate papillæ, the tip and margins, the glosso-palatine arch, with the soft palate and uvula. There is a portion on the centre of the dorsum which seems to be devoid of taste bulbs. The glosso-pharyngeal is the nerve of taste for the posterior third, and the lingual and chorda tympani for the anterior two-thirds of the tongue, though it is more than probable that all the gustatory fibres are originally contained in the ninth nerve.

The sensation of taste results when sapid substances dissolved in the fluids of the mouth are brought in contact with the gustatory cells of the taste-buds. Such substances are classified as (1) sweet, (2) bitter, (3) acid, (4) saline and (5) sour. Acid and saline substances at the same time stimulate the nerves of ordinary sensation if their solutions be of sufficient strength. Vintschgan maintains the existence of two primary tastes only, viz., bitter and sweet.

When a constant current is applied to the tongue, a sense of acidity is experienced at the positive pole, and of alkalinity at the negative, and this appears to be independent of the formation of electrolytes, for it takes place even when unpolarisable combinations are employed; and, moreover, the alkaline taste is experienced though the tongue be moistened with acid. The latter experiment, however, is not quite conclusive, as electrolytes may be produced, not in the fluid of the mouth, but in the tissues, and the nerve endings thus stimulated.

In testing the sense of taste the tongue should be protruded and dried and the eyes closed. The substance tested with may be applied on a camel-hair brush, care being taken to limit the application to one place, and to rinse the mouth with water between the experiments. The greater the surface of application and the stronger the solution the more intense is the resulting sensation. Quinine may be used in testing the taste for bitters, common salt for salines, acetic acid for acids, and sugar for sweets. The most persistent *after-taste* is produced by bitters, such as quinine, and these are also the slowest to be appreciated after application.

The sense of taste is sufficiently delicate to perceive one part of sulphuric acid in 1000 of water. It may be cultivated by

practice. Sweet and sour tastes are appreciated best at the tip of the tongue, acid at the sides, and bitter posteriorly.

If an extract prepared from the Gymnema Sylvestre be applied to the tongue, sweet and bitter tastes can no longer be perceived.

The Sense of Touch.

The sense of touch may be taken to include those of mere contact, of pressure, and of temperature changes. These sensations are appreciated through the skin and mucous membranes, and there are end-organs to receive the impressions, which show a considerable diversity of structure. This would *prima facie* lead us to suppose that the sensations were the result of stimulation of different nervous elements, *i.e.*, that each of these subdivisions of the sense of touch has a separate nervous path; and some of the phenomena of disease point to the same conclusion. Thus in locomotor ataxia, in which the sensory tracts are involved, tactile sense may be abolished and thermal sense left, or the muscular sense may be lost while the tactile sense is comparatively unimpaired. But though we may conclude that the evidence on the whole is in favour of the view that the skin is supplied with different kinds of nerve-fibres, some related to the sense of contact, others to that of pressure, and others again to that of temperature changes, we are unable at present to differentiate the various nervous paths.

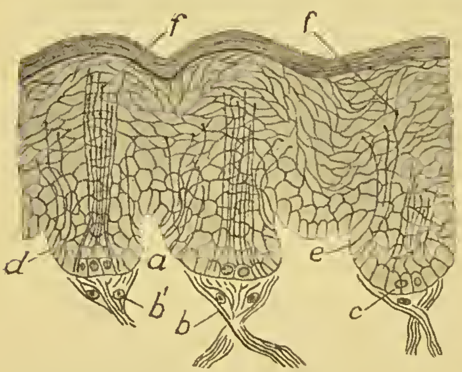

Fig. 373.—Vertical Section of Epidermis of Nose of Mole, to show Rimer's Organ.

a, Down-growth of epithelium; *d*, leash of nerve-fibrils; *f*, nerve-fibrils terminating in knobs; *e*, nerve-fibrils entering sides of down-growth.

Pain and the muscular sense cannot be regarded strictly as touch sensations, but they may conveniently be considered under the heading of touch.

The peripheral end-organs concerned in receiving impressions occur in the skin, mucous membranes, and subcutaneous tissues, and may be referred to shortly here.

General free endings are found in the epithelium of the skin

and cornea. The nerve-fibrils, after passing through the basement membrane, terminate between the cells in free points or small knobs. In the skin and hair-follicles they are limited in their distribution to the stratum Malpighii, while in the epithelium of the cornea they form a distinct network. A good illustration of this form of nerve ending is afforded by the *organ of Rimer* in the nose of the mole. Here a pencil of fibrils pierces a downward prolongation of the epidermis, and reaches nearly to the stratum corneum, the fibrils showing varicose thickenings, and ending in small knobs. In the snout of the pig an axis-cylinder or a division of it pierces the basement membrane, and divides into fibrillæ, which branch in the lower layers of the stratum Malpighii, and terminate in nucleated somewhat semi-lunar discs, each of which supports an oval tactile cell.

Special tactile organs.—1. **Pacinian corpuscles** are found in the loose tissue between the cutis vera and subjacent structures, about the joints, especially in the hands and feet, and in the periosteum of bones; in the mesentery (*e.g.*, of cat), in the capsule of lymphatic glands, in the pancreas, thyroid gland, &c. They are comparatively large and oval in shape, about one-twelfth inch in their long, and half as much in their short diameter, and consist of a number of concentric laminæ around a central cylindrical core, through which the termination of the axis-cylinder of the nerve-fibre passes. The lamellæ consist of delicate white and elastic fibres in a hyaline ground substance, and for the most part are continuous with the perineurium of the nerve-fibre on which they occur, and separated from each other by lymph-spaces lined with epithelioid cells. The central cylinder of the corpuscle exhibits a homogeneous ground substance with granules or nuclei in its outer part. The nerve-fibre entering one of the poles of the corpuscle retains its medullary sheath till it reaches the core, which it traverses as a naked axis-cylinder till it terminates in a thickened extremity at the other pole. The axis-cylinder may, however, bifurcate in

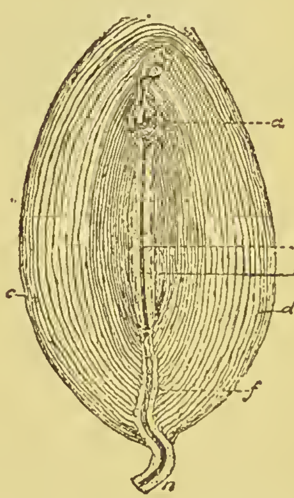

Fig. 374.—Pacinian Corpuscle from Mesentery of Cat.

n, Nerve-fibre in sheath of Henle; *n'*, its continuation through the core *m* as a naked axis-cylinder; *a*, termination of nerve; *d*, lines of separation of tunics; *c*, external lamellæ; *f*, canal through lamellæ traversed by nerve-fibre. (Ranvier.)

its passage through the core, and its termination may be broken up into processes.

2. **Wagner's corpuscles** occur especially in the papillæ of the palmar surface of the fingers and toes, and are about $\frac{1}{300}$ inch in length and $\frac{1}{800}$ inch in breadth. They are often pyriform in shape, with the broad end directed to the surface. According to some, one of these corpuscles has the following structure:—It is composed largely of a connective tissue basis in the form of a capsule, from which transverse septa, more or less complete, pass inwards. The nerve-fibre (or there may be more than one) loses its grey and medullary sheaths as it reaches the proximal end of the corpuscle, and at once, or, as is more usually the case, after first winding round the connective tissue basis, passes into its substance and gives off transversely running branches between the connective tissue septa, which terminate in round or oval enlargements near the periphery of the organ. Another view states that the corpuscle consists of a series of superimposed cells similar to those of Grandry's corpuscle, immediately to be described, enclosed in a capsule continuous with the perineurium of the nerve-fibre. The transverse markings, according to this theory, are due to branches of the nerve-fibre running horizontally between the adjacent cells, and terminating in enlargements comparable to Grandry's end-plates. Wagner's corpuscles do not occur in all the papillæ of the parts where they are found, and the papillæ in which they occur are said to be non-vascular.

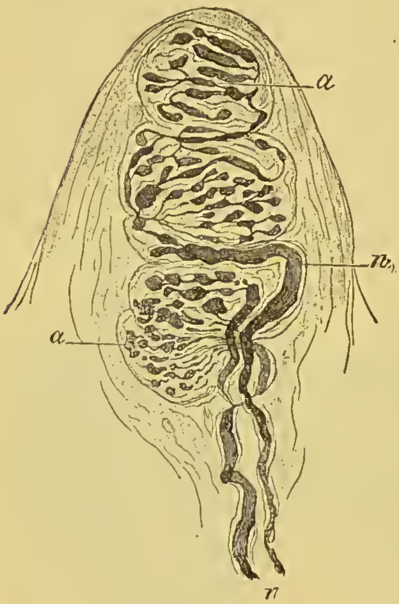

Fig. 375.—Wagner's Corpuscle.

3. **End-bulbs** is the name given to certain terminal organs found in the subepithelial tissue of the conjunctiva, of the lips, mouth and rectum, and of the glans penis and clitoris. A conjunctival end-bulb is spheroidal in shape, and possesses a core and a capsule. The former consists of polygonal or oval nucleated cells, amongst which the axis-cylinder (or cylinders) terminates. The outer fibrillated portion of the capsule is continuous with the sheath of Henle of the nerve-fibre, while the

inner nucleated membrane is continuous with the grey sheath. The medullary sheath stops when the bulb is reached, the axis-cylinder alone entering the corpuscle, to end, after a tortuous course, in a thickened extremity among the cells of the core.

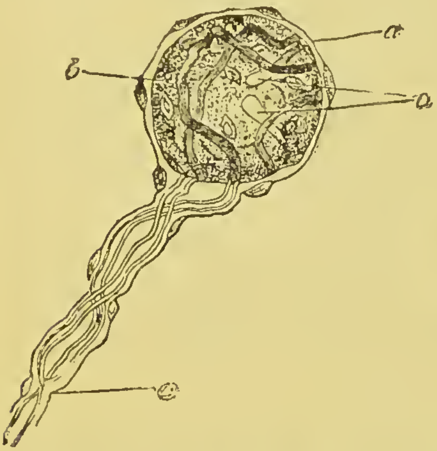

Fig. 376.—END BULB FROM HUMAN CONJUNCTIVA (HIGHLY MAGNIFIED).

a, Nucleated capsule; *b*, core; *c*, nerve; *d*, terminations of nerve. (Longworth.)

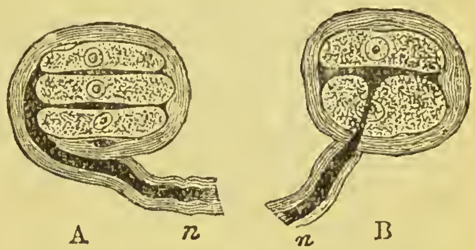

Fig. 377.—GRANDRY'S TACTILE CORPUSCLES FROM TONGUE OF DUCK (STAINED WITH GOLD CHLORIDE).

A, Composed of three cells with two intervening discs in which the axis-cylinder of the nerve *n* ends; *B*, composed of two cells with one intervening disc. (Ranvier.)

Grandry's corpuscles, which occur in the subepithelial connective tissue in the mouth of the duck and other aquatic birds, are invested with a fibrous capsule, continuous with the perineurium of the nerve-fibre, lined by a single layer of flattened nucleated cells continuous with the sheath of Schwann. Within this are two or sometimes three cells, nucleated, slightly granular and disc-shaped, their flattened surfaces separated from each other by a biconvex *tactile plate* lying between them. The nerve-fibre loses its medullary sheath as it enters the corpuscle, and the axis-cylinder is continued alone between the capsule and the cells. At the level of the interval between the cells it passes between them to join the tactile plate.

Sense of contact—localisation of tactile impressions.—Mere contact, as when the skin is lightly touched with a blunt instrument, gives rise to the simplest form of tactile sensation. Some parts, such as the tip of the tongue and the palmar surface of the forefinger, are more sensitive than others, and require a smaller minimum of pressure to produce sensation. Our ability to localise tactile sensations is determined by the power possessed by the skin of any particular part of distinguishing as a double

sensation the effect produced by contact with two points near together. The eyes are closed in testing this sense, and the impressions made with a pair of compasses: the greater the acuity of the sense, the nearer may the points of the compass be fixed, and yet a double sensation perceived. The following table shows the difference in tactile sensibility of various parts:—

	Least distance at which the points of a pair of compasses can be distinguished separately.
Tip of tongue	1·1 mm.
Palmar surface of third phalanx of forefinger	2·2 "
Tip of nose	6·7 "
Palm of hand	10·0 "
Back of hand	25·0 "
Gluteal region	37·0 "
Back of neck near occiput	50·0 "
Middle of thigh	62·0 "

The sense of locality varies with the number of tactile nerves in the particular part of the skin, and this, according to Weber, is due to the fact that the mind estimates the distance between the two points of the compass by the number of intervening unexcited endings. The acuity of the sense may also be greatly improved by exercise, as in the case of the blind who are able to read raised type with their fingers; and as the increased sensitiveness ensues on both sides we may conclude that the change is central and not peripheral. The motility of the part has a relation to the acuity of perception which is greater in the skin of the fingers and toes than in the less peripheral parts of the limbs. It is worthy of note, too, that in the limbs the sensitiveness is greater in the transverse than in the long axis, so that the points of the compass to be recognised separately require to be further apart when they fall in the long than when they are in the short axis.

Moistening the skin increases the acuteness of perception.

The internal organs as a rule are destitute of tactile sense.

The **sense of pressure** enables us to estimate the amount of weight or pressure upon the skin. It is, however, differently distributed to that of contact. Thus the forearm is as sensitive to pressure as the palm of the hand, nor is the tongue the most discriminative part for pressure.

It may be well here to define what is meant by the *fraction of discriminative sensibility*. This depends on the increase or decrease of stimulus necessary to produce an increase or decrease of sensation. According to Weber the relation between the stimulus and sensation may be stated as follows:—*Whatever the absolute strength*

of a stimulus of given kind may be, it must be increased by the same fraction of its amount in order that a difference in the sensation may be perceived. For example, in the case of light it is found that if an increase in the impression produced by 100 lighted candles is to be perceived at least one candle must be added; if a decrease, at lease one candle must be taken away. The fraction of discriminative sensibility is therefore $\frac{1}{100}$th, and this fraction applies whatever the amount of the stimulus may be, that is to say, within certain limits. If the original stimulus be that of 1000 candles, one candle added or taken away no longer produces the same effect as when only 100 were used—the difference is not perceived and it is found that we must add or subtract $\frac{1}{100}$th of the original stimulus, *i.e.*, 10 candles, before there is an increase or decrease of sensation. In other words, the fraction of discriminative sensibility for light is $\frac{1}{100}$th, and each of the senses is found to have its own fraction. Thus for sound it is one-third, for the muscular sense

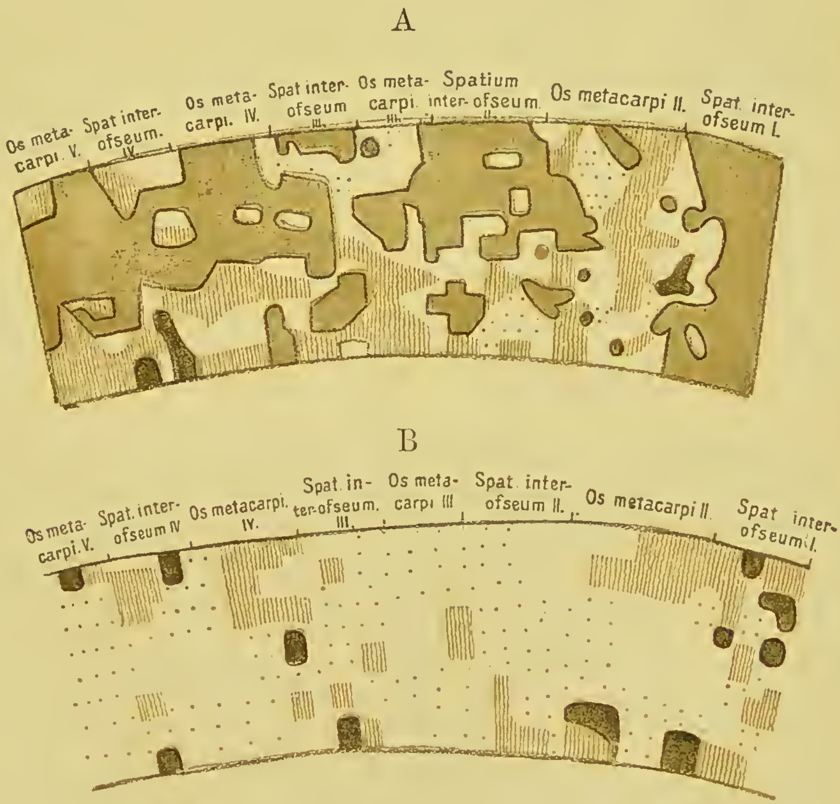

Fig. 378.—Map of Hot and Cold Areas of Middle Region of Back of Hand.

A, Cold areas. B, Hot areas.

one-seventeenth, for temperature one-third, and for pressure one-sixth at the finger tip to one-third at the shoulder blade.

The **sense of temperature.**—By this sense we are able to recognise variations in the temperature of the skin, so that a feeling of cold results if a body applied to the skin surface withdraws heat from it, and a sense of warmth if heat be communicated to it in a similar way. It is thus changes of temperature more than the absolute height which we appreciate. Here, again, the distribution of the sense shows differences in acuteness in different parts, the tip of the tongue, eyelids, cheeks, lips, neck and body being sensitive in the order given. As has been stated, the fraction of discriminative sensibility is about one-third. But the distribution of the temperature sense is peculiar in that the whole skin surface in any one part is not uniformly sensitive. There is apparently an end-apparatus for this sense arranged in a punctuated manner—in the form of "temperature spots" scattered over the skin, some of these being "hot spots" and others "cold spots." The hot spots give a sensation of warmth when touched with a warm instrument but are insensitive to a cold one; while the cold spots respond to a cold stimulus but not to a hot one; and the cold spots are the more numerous of the two. The accompanying figure after Goldscheider shows maps of these "hot" and "cold" areas, the dark parts being the most sensitive, the shaded to a less degree, the dotted feebly, and the blank spaces not at all (Fig. 378).

The mucous membranes of the body are comparatively insensitive to temperature changes, or altogether so, as is the case with the greater part of the alimentary canal; and the internal organs as a rule are devoid of this sense.

Muscular sense has been defined by Bowditch as "The appreciation which we have of the intensity and direction of muscular effort." It was at one time believed to be an entirely central or psychical process, in which a mental estimate was made of the amount of energy expended in the performance of any definite act; an estimate necessarily founded on data formed by past experience. While this conception is probably quite acceptable to a certain extent, still a considerable amount of evidence has been accumulating which would show that the sense is largely a peripheral one. Thus if a load be attached to the fingers, and the muscles stimulated, not by an effort of will, but by faradic stimulation of the arm, there is immediate perception of the amount of the weight, &c., though the cerebral cells have not been required to send out motor impulses to contract

the muscles. Again, many histologists and physiologists have demonstrated the existence of special terminals in tendons, muscles, fascia, periostia and the skin which seem to be concerned in the production of centripetal impulses which pass to the central nervous system.

Ciaccio's researches prove the existence of sensorial terminals lying among the longitudinal bundles of white fibres which compose the tendon bundles. Probably the most important terminals, however, are the neuro-muscular spindles which are found more especially in the muscle near the tendinous insertions and in the inter-muscular septa. Sherrington has conclusively shown that the ordinary, apparently motor, nerve which goes to supply a muscle contains a very large proportion of afferent fibres, and it appears as if these were connected with the spindles we have just mentioned. The terminals vary very considerably in size and complexity in the different classes of animals. In the frog, lizard and snake they are of a very simple type. They consist of a fibrous and somewhat dense sheath which encloses a single muscular fibre; the central part of which seems to consist of feebly differentiated protoplasm, rich in nucleated plate-like cells, while the poles of the fibre show the ordinary striation of muscle, though somewhat fainter than is normally the case. One pole may be directly continued in a tendinous bundle. Between the capsule and the muscular fibre lies a lymph space, best seen in the central part of the spindle and containing the nerve which has pierced the capsule, and which has generally, though by no means always, lost its medullary sheath. The axon then breaks up into a nervous plexus which, according to Ruffini, may be of several types. Of these the most important apparently is a spiral, enclosing the muscular substance. In the higher types of mammals, and more especially the apes, the spindles are very large and may contain several muscular fibrils, with the axones arranged in leaflets between the fibres, or they may be arranged in the annulo-spiral arborescence just described.

Fig. 379.—Neuro-Muscular Spindle.

Many other sensory terminals are not infrequently found in muscle, such as Pacinian corpuscles, but it is doubtful whether they are concerned in muscular sense.

It is probable that impulses are generated in the muscle and

tendon during muscular activity, as in lifting a weight, which are then transmitted along the "motor" nerves to the spinal cord, the cerebrum and cerebellum, there to participate in the complex nervous processes underlying the phenomena of equilibration, co-ordination, &c.

It is more than probable, also, that somewhat similar impulses are transmitted from the sensory terminals found in other areas which are especially exposed to variation in muscular tension, such as periostia and even bone. It is extremely difficult to conjecture the method by which the various terminals receive their stimuli, though, in the case of the neuro-muscular spindle, it might be thought that they were derived from variations of tension in the muscular fibre enclosed within the sensitive nervous spiral.

It is also to be remembered that in one respect muscular sensation is especially acute, for whereas the fraction of discriminative sensibility in an ordinary tactile sense is one-third to one-sixth, that of muscular sensation is one-seventeenth.

Pain is caused by a higher stimulation than normal of sensory nerves, and may be the result of mechanical, thermal, chemical, electrical or other stimuli applied to the organism. It follows sufficient stimulation of a sensory nerve at any part of its course, but the sensation is referred by the mind to the area of its peripheral distribution.

The skin is *par excellence* sensitive to pain, the deeper parts being comparatively insensible, in fact, the pain of an operation without anæsthetics is almost limited to that experienced during the incision of the skin and the subsequent stitching up of the wound. But though muscles, both striped and non-striped, are insensitive to cutting, violent contractions of the hollow viscera, *e.g.*, œsophagus, stomach, intestine and uterus, may cause very great pain indeed; and the pain suffered in cramp of the voluntary muscles is familiar to all.

These considerations would lead one to suppose that the path of painful sensations may be distinct from that of tactile ones, for the hollow viscera, as we have seen, are usually destitute of tactile perception. Moreover, in disease sensibility to pain may disappear while the sense of touch remains, and *vice versa*.

CHAPTER XVI.

VOICE AND SPEECH.

VOICE is produced in the larynx, an organ composed of several cartilages joined together by membranes. The cartilages have a certain power of movement through the action of muscles inserted into them. Inside the larynx lies a pair of membranous structures — the true vocal cords — which vibrate under the influence of a blast of air expelled from the lung during expiration, producing sound. As the anatomical relations of the various parts are of great importance, it is necessary for the student to study them somewhat fully.

Cartilages.—These are nine in number, three being paired and three unpaired:—

Unpaired	Thyroid. Cricoid. Epiglottis.	Paired	Arytenoids. Cartilages of Santorini. Cartilages of Wrisberg.

Thyroid. — It consists of two wings or alæ which join in front but remain separate behind. The alæ at their junction form a swelling—the pomum Adami—often very pronounced in the male; immediately above the pomum is a notch filled in by the thyro-hyoid membrane. The outer surface of the cartilage gives attachment to some of the extrinsic muscles of the larynx. The superior and inferior borders are prolonged at their posterior ends into processes or cornua, of which the superior passes upwards and inwards to give attachment to the thyro-hyoid ligaments, while the inferior, shorter and thicker than the superior, project downwards to articulate with facets on the upper border of the sides of the cricoid cartilage. The internal surfaces are smooth, concave, and covered by mucous membrane, and join in front, forming an angle of from 80 to 90 degrees. Posteriorly the space between two alæ is partially filled in by the thickened portion of the cricoid cartilage with the two arytenoids.

Cricoid.—This is a ring-shaped cartilage lying immediately

below the thyroid: the ventral portion is narrow and rounded, while the posterior is thick and square; it shows on its upper surface two oval facets for articulation with the arytenoid cartilages, separated by a small depression. The superior border of the lateral part of the cartilage, with the surface immediately below, gives origin to the crico-thyroid muscle; while in front the border becomes rounded and affords attachment to the central portion of the crico-thyroid membrane. The posterior aspect of the cricoid shows a vertical line with a smooth slightly-depressed surface on each side for the origin of the crico-arytenoideus posticus, with a facet a little in front for the articulation of this cartilage with the inferior cornu of the thyroid. This joint is of great importance in the production of certain vocal tones.

Arytenoids.—Two somewhat triangular cartilages with broad inferior surfaces which articulate with the facets on the upper surface of the posterior part of the cricoid. They present three surfaces, of which the posterior is the most important as it gives attachment to the transverse fasciculus of the arytenoid muscle. Two distinct angles are present—an anterior, thickened to form the vocal process, and a postero-external or muscular; to the former is attached the true vocal cord and a few fibres of the thyro-arytenoideus, and to the latter the crico-arytenoideus lateralis in front and the crico-arytenoideus posticus behind.

Cornicula laryngis (cartilages of Santorini).—Two little cone-shaped bodies of elastic cartilage attached to the apices of the arytenoid, and not infrequently incorporated with them.

Cuneiform cartilages (cartilages of Wrisberg).—Also two small yellow elastic structures lying in the aryteno-epiglottidean folds.

Epiglottis.—This can hardly be considered a true cartilage of the larynx, though generally included with them. Like the cornicula it is composed of yellow elastic cartilage; the shape is an elongated oval, somewhat like a leaf with a stalk attached to the back of the thyroid cartilage; it presents two surfaces, an anterior or lingual facing the back of the tongue and covered by a reflexion of mucous membrane from that organ, called the glosso-epiglottidean fold, and a posterior, lying just above the superior aperture of the larynx, with a little swelling about its middle called the cushion of the epiglottis. The lateral borders of the cartilage in their lower portions are included in a well-marked fold of mucous membrane which passes back to the arytenoids and is therefore called the aryteno-epiglottidean fold (Fig. 384).

Ligaments and membranes of the larynx.—The most important are the lateral portions of the crico-thyroid membrane,

which assist in the formation of the true cords. The crico-thyroid membrane has two parts—a central portion joining the ventral aspects of the thyroid and cricoid cartilages together, and a lateral passing upwards from the upper border of the lateral aspect of the cricoid under cover of the thyroid in close contact with the mucous membrane of the larynx to end in the inferior thyro-arytenoid ligament or true vocal cord. The cords are two bands of fibrous tissue containing many yellow elastic fibres extending from the back of the thyroid cartilage immediately external to the middle line to the vocal process of the arytenoid; in the anterior part of the cord lies a tiny nodule of cartilage called the cartilage of Luschka. They are sometimes termed the inferior cords from the presence of two thick fleshy bands situated almost immediately above, and consequently called the superior or false cords.

Joints of the larynx.—The crico-thyroid and crico-arytenoid joints are both of great importance; the former consists of the articulation of the inferior cornua of the thyroid cartilage with a rough surface on the postero-lateral aspect of the cricoid. It acts as a fulcrum around which the two cartilages move on contraction of the crico-thyroid and thyro-arytenoideus muscles; in addition to this rotatory motion there is probably also a simple gliding movement of the one cartilage on the other.

The **crico-arytenoid** joint is formed by the articulation of the broad inferior surface of the arytenoid with the articular facet on the upper surface of the cricoid; it admits also of two types of movement—(1) a rotary movement around a vertical axis by which the vocal processes are brought together or separated, leading consequently to an adduction or abduction of the true cords, and (2) a lateral movement of the whole arytenoid cartilage on the articular facet, such as we obtain on contraction of the horizontal fibres of the arytenoideus.

Muscles.—The muscles of the larynx can be divided into two groups, the extrinsic and the intrinsic. The former group comprises the muscles passing from the thyroid cartilage to the sternum, hyoid bone, &c. These act either as elevators or depressors of the larynx and are only of indirect importance in voice production. The intrinsic muscles are the crico-thyroid, lateral crico-arytenoid, arytenoideus, thyro-arytenoideus, posterior crico-arytenoideus and a few others of minor importance.

Crico-thyroid.—The muscle arises from the front and sides of the cricoid cartilage below, the fibres being arranged in two fasciculi, the upper of which passes to be inserted into the lateral

ala of the thyroid, while the lower is attached to the anterior border of the inferior cornu. *Function.*—The articulation of the inferior cornu of the thyroid with the cricoid acts as a fulcrum on which the cartilages move on contraction of the muscle. When the fibres shorten the two cartilages are drawn together in front and separated behind, so that the distance between the posterior surface of the thyroid in front and the vocal process of the arytenoid behind must be increased, producing a rise in tension of the vocal cords.

Nerve supply to the laryngeal muscles.—All the fibres are derived from the pneumogastric through its superior and inferior laryngeal branches. While the former is essentially the sensory nerve of the larynx, it also gives off muscular twigs to supply the crico-thyroid muscle and part of the arytenoideus; all the other muscles are supplied by the inferior or recurrent branch.

Crico-arytenoideus lateralis.—It arises from the upper border of the cricoid cartilage as far back as the articulation of the arytenoid; the fibres sweep upwards and backwards to be attached to the front of the muscular process and the adjacent border. *Function.* — The muscle pulls forwards and downwards the muscular process and thus rotates the vocal processes inwards, leading to adduction of the cords.

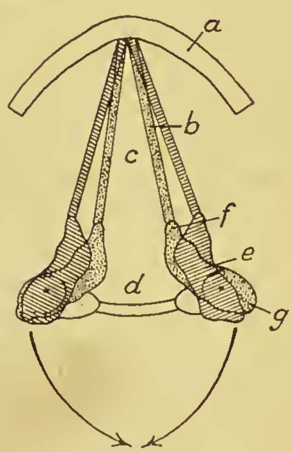

Fig. 380. — Diagram Illustrating Action of the Crico-arytenoideus Posticus (Abductor).

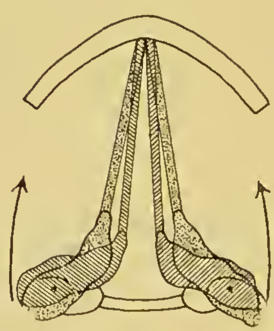

Fig. 381. — Diagram Illustrating Action of the Adductors.

Crico-arytenoideus posticus.—It is attached below to a large depression on the posterior aspect of the cricoid, from which the

fibres pass upwards to be inserted into the posterior aspect of the muscular process of the arytenoid. *Function.* — On contraction the muscle rotates the muscular process backwards around a vertical axis, so that the vocal processes swing apart, carrying with them the vocal cords.

Arytenoideus.—The muscle consists of two portions, an anterior fasciculus composed of transverse, and a dorsal one of oblique fibres. The ventral bundle passes between the large concave surfaces on the back of the arytenoids, while the posterior or oblique fibres sweep upwards into the lateral walls of the larynx and the aryteno-epiglottidean folds. *Function.* — Contraction of the anterior fibres must draw the arytenoid cartilages together, producing adduction of the vocal cords associated with a certain amount of depression of the cartilages, both actions being probably of especial importance in the production of tones of the higher registers. The oblique fibres may have something of a sphincter action.

Thyro-arytenoideus.—The muscle is arranged in two parts—an external and an internal—though the two blend to such an extent that they practically form one sheet. The *internal* fasciculus arises from the back of the thyroid at the side of the attachment of the vocal cords, and also from the anterior end of the vocal cord itself, where a little nodule of fibro-cartilage is situated (the cartilage of Luschka). The fibres are collected into a somewhat triangular bundle which sweeps backwards in a crescentic fashion to be inserted into the vocal process of the arytenoid and its adjacent anterior border. On the inner aspect of this band lie a series of short fibres arising from the outer and under part of the cord itself and attached to the vocal process. In addition to the antero-posterior fibres making up the bulk of the inner part of the muscle there are also many oblique fibres which pass upwards and outwards into the false vocal cords and the adjacent parts. The *external* fasciculus arises also from the back of the thyroid cartilage, and like the internal it contains two sets of fibres—antero-posterior and oblique; the former run directly backwards to the arytenoid, where they are inserted into the front of the muscular process, while the latter pass into the aryteno-epiglottidean folds. *Function.*—From the presence of so many different bands of fibres it will be obvious that the muscle has more than one function. The antero-posterior ones, for example, will pull the thyroid and arytenoid cartilages together and thus relax the tension of the vocal cords; the oblique ones will possibly participate in the sphincter action mentioned under the arytenoideus; while the innermost fibres arising from the vocal

cord itself and passing to the vocal process are employed in the production of the tones in the higher register. Further, the fibres attached to the muscular process must on contraction rotate the vocal processes inwards, procuring adduction of the true cords.

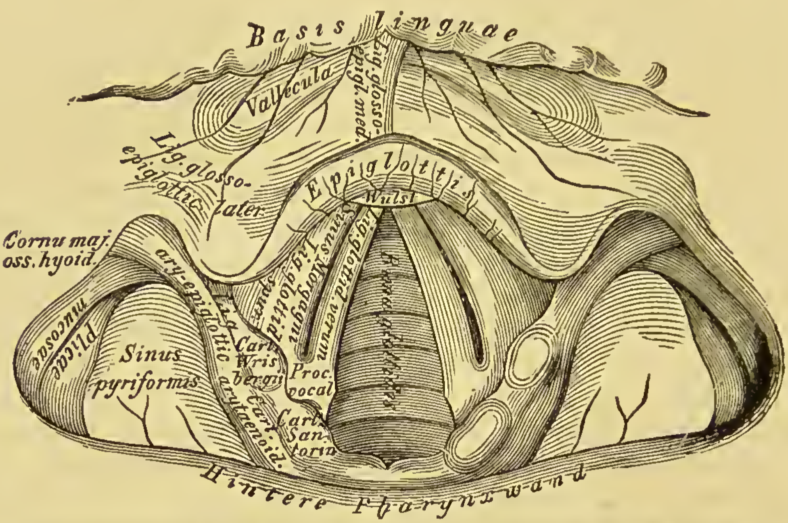

Fig. 382.—Laryngoscopic Appearance of the Interior of the Larynx.

The **interior of the larynx.**—The interior of the larynx communicates by an opening, called the superior aperture, with the larger cavity of the pharynx. The opening, which is situated somewhat obliquely, is bounded anteriorly and superiorly by the epiglottis, postero-inferiorly by the arytenoid cartilages, and laterally by the aryteno-epiglottidean folds. The interior is, moreover, divided into upper and lower segments by the presence of the true vocal folds; the upper, or laryngeal cavity proper, contains two rounded protrusions of mucous membrane called the superior or false cords, which can be readily distinguished from the true cords by their flesh-like colour and characteristic shape. Immediately beneath the false cords lie saccular dilatations, called the laryngeal ventricles of Morgagni.

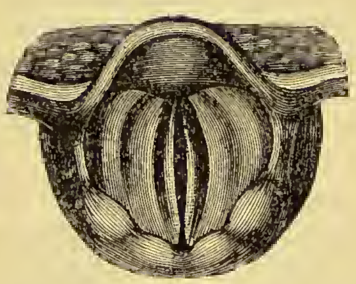

Fig. 383.—Position of the Cords in Adduction.

The **true vocal cords** are two pearly-white antero-posterior bands separated by a space or chink called the *rima glottidis;*

they extend from the back of the thyroid cartilage in front to the vocal process of the arytenoid behind. The length of the cord varies slightly in the different sexes, thus in the male it averages 16 mm. and in the female 12 mm. The rima glottidis may be divided into two parts, an anterior or interligamentous portion, the glottis vocalis, and a posterior portion between the arytenoid

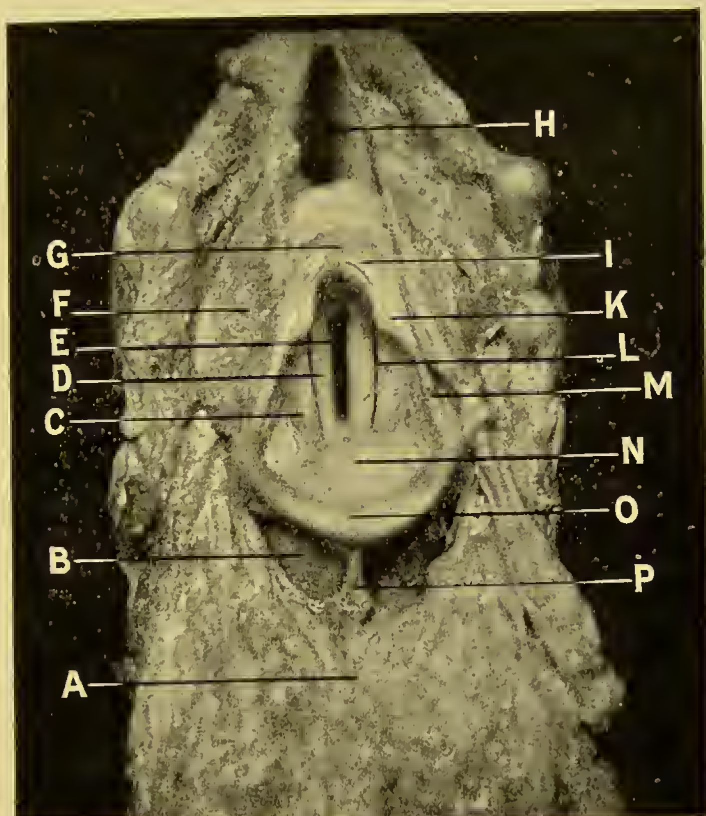

Fig. 384.—Larynx seen from above.

A Base of Tongue.
B Vallecula.
C False Cord.
D True Cord.
E Chink of Glottis.
F Sinus Pyriformis.
G Inter-Arytenoid Fold.
H Œsophagus.
I Arytenoid.
K Cartilage of Wrisberg.
L Opening of Ventricle of Larynx.
M Aryteno-epiglottidean Fold.
N Cushion of epiglottis.
O Epiglottis.
P Central Glosso-epiglottidean Ligament.

cartilages called the glottis respiratoria. The size and the shape of the space varies with the functional activity of the parts. In normal or quiet respiration, the movements are so slight as to frequently escape observation, but on forced inspiration the cords become widely separated, so that the glottic aperture becomes greatly increased in size.

The movement is due to the contraction of the crico-arytenoideus posticus. In paralysis of the recurrent laryngeal nerve the cords fall towards the middle line (cadaveric position) thus reducing the size of the glottic aperture.

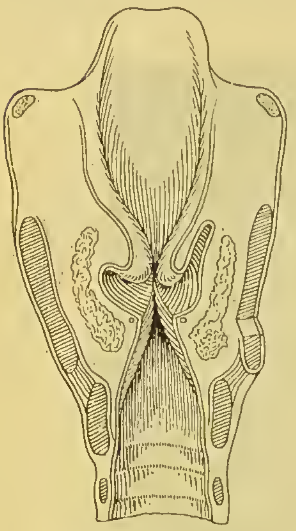

Fig. 385. — Longitudinal Section through the Larynx.

During forced respiration the triangular contour of the rima becomes markedly broadened so that the opening may become of a lozenge shape. In sound production, or phonation, on the other hand, the arytenoid cartilages are rotated forwards so that the cords become adducted and the glottic aperture reduced to a mere chink.

Voice and Speech.

Sounds may be divided into two classes, musical and non-musical; in the former the waves are rhythmic, whilst in the latter they are irregular. The waves consist of ethereal vibrations arranged in alternate phases of condensation and rarefaction, and are produced by the regular movement of some elastic body, such as a reed or cord; if the vibrations be too few in number no sound is produced, but as their frequency increases musical tones, gradually rising in pitch, are produced, until the sound ceases to be musical. Musical sounds range from a low tone produced by thirty vibrations per second to one of great height (some thousands), when the musical quality disappears.

Fig. 386.—Position of the Cord in Forced Inspiration.

If the action of a vibrating cord be studied it will be noticed that in the first instance the cord oscillates as a whole, producing a fundamental or essential tone, from which we get the pitch of the note, and in the second place that it vibrates in segments of half, quarter, &c., of its length, each segment producing a tone which we call a partial or overtone. If, for example, the whole cord produces a fundamental tone corresponding to C with 132 vibrations, then the partials or segmental tones will have vibrations in direct numerical ratio to that number, viz., 264, 396, 528, &c. The

greater the number of partials produced the richer is the quality of the complete note or klang; in some tones, such as those of the clarionet or trumpet, the harmonics are particularly well marked, giving them a characteristically brilliant quality, whilst in others (flute, &c.) the overtones are much less prominent, so that a softer tone is obtained. Sounds of all types travel at 1100 feet per second, hence if we know the number of vibrations in the tone we can calculate the wave length: thus in a note of eleven vibrations the length will be 100 feet per second, in one of 55 vibrations the wave length is 20 feet, &c. If instead of a cord a membrane be thrown into vibration the overtones may not preserve the strict arithmetical relation to one another just described, so that some of the overtones may tend to disturb the perfectly musical nature of the note, more especially if the inharmonic tones approximate in pitch to the fundamental one. If two tones of slightly different pitch be sounded simultaneously, it will be apparent that the vibrations of the two being different will have unequal wave lengths, so that at one time the phases of condensation will coincide, when a marked increase in volume is obtained, while a little later the condensation of one will be synchronous with the rarefaction of the other, when the tone is diminished. Thus we have a series of variations in intensity resembling pulsations, called *beats*. The number of beats per second corresponds to the difference in the frequency of the vibrations of the two notes, thus, if the first has 132 vibrations and the second 198 vibrations, then the beats will be sixty-six per second, and this frequency is so considerable that a new tone becomes developed, called the differential tone, which in some cases is very well marked. If the two tones are of nearly the same pitch the result may not be unpleasant, but if they be widely separated the large number of beats which are produced renders the compound tone disagreeable. If the second note has a numerical frequency in direct ratio to that of the first, then no beat will be produced, and the two tones are said to be in perfect concord or harmony, while if this relation be departed from, discord or dissonance results. The harmony of a common chord may be taken as an example—

	C	E	G	C′
Vibrations	132	165	198	264
Ratios	4	5	6	8

Analysis of compound tones.—If a compound tone be sounded near an open pianoforte with the damper raised, it will

be found that a number of the wires vibrate in response to the component fundamental and harmonic tones. Helmholtz employed a series of metallic chambers or resonators, roughly cylindrical in shape, but pointed at one end for insertion into the ear, and with a rounded opening at the other for the reception of the sound waves. When a compound tone is sounded in the vicinity of the resonator, the particular fundamental or overtone corresponding to the instrument is picked out by it, amplified in the cavity of the chamber, and recognised by the ear.

Fig. 387.—HELMHOLTZ RESONATOR.

By means of a series of resonators the components of a complex tone can be made out, and if the chambers be connected to manometric capsules a flame analysis can readily be made.

The manometric capsule invented by König is simply a small chamber divided into two parts by a membrane; the one half communicates by means of a tube with a mouthpiece for the reception of the sound waves, whilst the other contains ordinary gas supplied by a small inlet pipe, and connected to a little jet where the gas can be ignited. The vibrations of the air in the first chamber are transmitted through the membrane to the gas in the second, when the flame assumes peculiar and characteristic shapes.

Musical tones have three characteristics—viz., Pitch, Timbre and Volume.

Pitch.—This depends entirely on the frequency of the vibrations produced; thus the lowest note of the pianoforte (A) has a frequency of only 27·5 vibrations per second, while the highest (C) has over 4000. The range of the human voice is of course much less, the lowest recorded tone being that of Forster, $F_{,,,}$ (42 vibrations), and the highest that of Madame Ajugari, recorded by Mozart, C'''' (2048 vibrations). The ordinary range of any one voice is about two octaves. In the case of an ordinary vibrating cord, pitch depends on two factors, viz., the length and the tension of the cord, thus the greater the length and the less the tension the lower the tone. This is not the case, however, with the vocal cords, where the vibrating elements become actually lengthened as the pitch of the tone rises, so that the rise in the

number of the vibrations must be due to the increase in the tension and perhaps to a thinning of the cord.

Timbre, or tone-colour, depends chiefly on the number, nature and prominence of the partial tones. If a considerable number of these be not in perfect harmony with the fundamental tone they impair the purity of the whole note and consequently produce an unpleasant effect.

Volume depends on the amplitude of the vibrations and therefore largely on the force of the expiratory effort, and to a lesser extent on the size and management of the resonating chambers.

Production of sound.—The trachea is a tube with a superior opening—the glottis—bounded by two elastic bands—the vocal cords—into which muscular fibres are inserted. As the air is driven through the opening during expiration the cords act as interrupting agents and throw it into vibrations, which pass upwards into the resonating chambers of the pharynx, mouth, nose, &c., there to acquire characters which assist in the production of the characteristic compound musical tone. If the cords be widely separated, as in respiration, the interruption to the passage of the air does not occur, so that no sound is produced; while, on the other hand, the greater the adduction of the cords, the more marked will be the interruption, and as at the same time the tension of the cords is increased the pitch of the tone necessarily rises. It will be evident, also, that in the latter instance a greater force will be required to open the vocal cords, and if the intra-tracheal pressure be estimated with a manometer this will be found to be the case, the pressure varying from 10 mm. Hg. in the production of a low tone to one of over 80 mm. in the case of the highest notes.

The increase in the tension of the cord is produced by contraction of the crico-thyroid muscle. When the muscle shortens, the distance between the thyroid cartilage in front and the arytenoid behind becomes increased, so that the tension of the cord stretching between these two points becomes increased. This, however, cannot explain the whole of the process, as the increase in length and tension cannot be considered sufficient to account for a rise in pitch of over two octaves. Also, if a scale be slowly sung it will be noticed that at certain points breaks occur, accompanied with a sensation of strain, immediately followed by a feeling of relief as the voice rises to the next note; when this occurs the voice is said to be passing from one register to another. The exact number of these registers is doubtful,

though most physiologists believe that there are three—(*a*) a low, thick, or chest register, employed in the production of the lower tones of the voice; (*b*) an intermediate; and (*c*) a head register used in the formation of the highest tones. These registers are better marked in the male than in the female. It is believed that in the lowest register the cords vibrate throughout their whole length and thickness, including, to a certain degree at least, the arytenoid cartilages themselves, the rise of pitch in the notes of the register being produced through the contraction of the crico-thyroid. As the pitch rises the crico-arytenoideus lateralis rotates the arytenoid cartilages so that the vocal processes become gradually approximated.

When the middle register is employed the anterior ends of the cartilages are in contact, so that only the cord proper is able to vibrate, while in the case of the highest or head register it seems as if the posterior portion of the vocal cord was fixed by the contraction of the innermost fibres of the central fasciculus of the thyro-arytenoideus so that only the anterior segment of the cord is allowed to vibrate.

The rise of pitch in each register is produced by contraction of the crico-thyroid, and the sensation of relief experienced when the voice passes from the one register to the next is due to the relaxation of this muscle. In the male the cords are considerably longer and thicker than in the female, hence the tone is deeper; in childhood the cords are somewhat similar in the two sexes, but at puberty in the male there is very decided growth in both the length and the thickness of the cord, when the voice is temporarily lost or broken. After the development of the voice is completed, the quality may be either light or flexible as in the tenor and soprano, or full and sonorous as in the contralto and bass.

Speech is made up of two types of sounds—vowels and consonants; the former can be classed among musical sounds, while the latter generally are not. *Vowels* are formed in a manner precisely similar to other musical tones—by a vibration of the vocal cords and an amplification of the sound in the resonating chambers. The vowels are *a* (ah), *e* (ee), *o*, *u* (oo), *i*. If the vowels be sounded in succession, it will be noticed that the pitch of the tone seems to rise, *a* being apparently the lowest and *i* the highest. Helmholtz found that if the mouth be arranged in the position normally assumed in the production of any specific vowel with the lips widely separated, and a series of tuning forks then sounded immediately in front, the oral cavity could be felt to respond most perfectly to the vibrations of one special tuning fork, thus determining the pitch of that vowel; when the shape of the

mouth was changed for the production of another vowel it no longer responded to the same fork but to another of different pitch.

Through the use of the phonograph as a recording instrument new methods of investigation have been employed by Hermann, M'Kendrick and others. Records of vowel tones are obtained, called phonograms, which are later carefully analysed.

Hermann maintained that the fundamental tone is constant but that the characteristic timbre, &c., was derived chiefly from the presence in the tone of a special predominating partial, which is termed the formant, and which need not be, and in point of fact generally is not a true harmonic or even a musical note at all. Later work by Sauberschwartz supports strongly the importance of the formants, and indeed seems to prove that we very commonly have more than one formant present, and that while

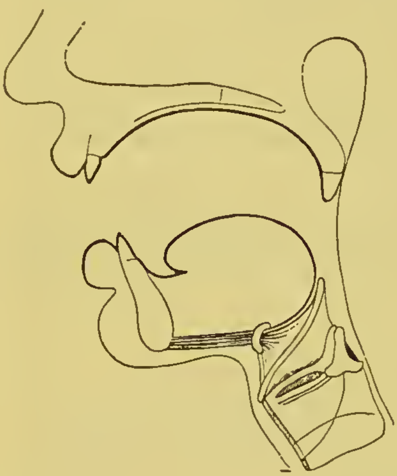

Fig. 388.—Position of the Tongue in the Production of the Vowel *ā*.

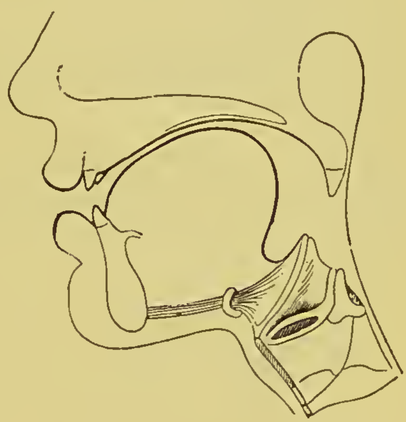

Fig. 389.—Position of the Tongue in the Production of the Vowel *e*.

one might be removed without destroying entirely the character of the vowel, removal of both at once produced this effect. It might therefore be assumed that while the fundamental tone is produced by the cords in the usual way, the characteristic element is due to these special formants formed in the resonating chambers themselves. The most important of these chambers is certainly the cavity of the mouth, which alters considerably in the production of the different vowel tones. In *ā* the tongue is depressed, so that the cavity of the mouth is as large as possible, while the lips are widely separated. For *e* the tongue is arched

very high, so as almost to touch the palate, while the lips are drawn baekwards as in smiling. In *o* and in *u* the tongue is raised at the back and hollowed at the front, so that a somewhat flask-shaped eavity is obtained, while in the latter vowel the lips are protruded.

Consonants are due to interference with the eurrent of air as it passes outwards through the respiratory passages; the obstruction may be produeed in certain situations, called by Brücke the artieulation positions.

1. At the lips, which are burst apart in the formation of the consonants—*p*, *b*.
2. At the anterior part of the mouth by the approximation of the tongue to the teeth and palate—*d*, *t*, &e; if the point of the tongue vibrates in addition we get *r*.
3. At the back of the mouth, between the tongue and the soft palate—*k*, *g*.
4. At the glottis as—*n*, *m*, and *ng*, though in this instanee the sound is intensified by vibration produced in the nose and pharynx.

They may be classified also according to the nature of the sound and its method of origin into explosives, aspirates, vibratives and resonants.

Explosives—		Vibratives—	
1st Position	b, p.	1st Position	o.
2nd Position	t, d.	2nd Position	r.
3rd Position	k, g.	3rd Position	r (palatal).
		4th Position	r (Lower Saxon).
Aspirates—		**Resonants—**	
1st Position	f, v.	1st Position	m.
2nd Position	s, z, l, sch, th.	2nd Position	n.
3rd Position	j, ch.	3rd Position	ng.
4th Position	h.	4th Position	o.

Stammering and stuttering.—The former is an inability to control diaphragmatic movement, so that breaks occur in the relaxation of the muscle and consequently the expiration is jerky; it is commonly found in very nervous subjects or in cases of great mental exeitement. In stuttering, on the other hand, the fault lies in the sound-produeing mechanism and is not related in any way to the respiratory muscles.

CHAPTER XVII.

THE NERVOUS SYSTEM.

THE nervous system is composed of two distinct structural elements, one nervous and the other supporting. The nervous element consists of nerve-cells and fibres, though it must be carefully borne in mind that the fibres or processes are mere outgrowths of the cell, and must be considered portions of its substance. The term nerve-cell should, strictly speaking, cover both the body of the cell and the processes coming from it, but as the custom of restricting the term to the cell body alone is so well established, and in many ways so convenient, it will be advisable for us to follow it and to employ the term "neuron" to indicate the complete nerve unit. The nerve-cells are found almost entirely in the grey matter of the brain and spinal cord, whilst the fibres are present in both the grey and the white substance. The cells and their fibres are supported by a framework of neuroglia. The arrangement of the elements in the central nervous system can only be ascertained by careful macroscopic and microscopic examination of sections through its various parts. In the preparation of the microscopic specimens special methods are employed which enable us to trace the course pursued by the various bands of fibres and to ascertain the characters and connections of the nerve-cells in the various parts. Of these, the silver chromate method of Golgi must be considered of first importance, though, as we shall see later, the deductions drawn from its employment may not be entirely acceptable. The reagent stains the cell and its processes an intense black, and the method is so remarkably delicate that even the finest fibrillæ appear as distinct black threads.

In 1891 Professor Waldeyer formulated the neuron theory, which has been very generally accepted both by physiologists and anatomists. The theory holds that each nerve-cell with its processes forms one distinct nerve unit, and that the whole of the central nervous system is composed of such units, which are

functionally, though not anatomically continuous with one another. Each process ends in an arborescence which interweaves with similar terminals derived from other neurons, so that nervous impulses can be readily transmitted from one unit to others; this functional connection between processes, or between cell and processes, has been termed by Foster a "synapse." The chief difficulty in our acceptance of this, or indeed any theory, lies in our ignorance of the actual factor in the cell or fibre which transmits the impulse: Leydig holds that it is the inter- or peri-fibrillar substance, though it is more generally believed to be the fibrillæ themselves. As we shall see later, Apathy has demonstrated in the annelids the passage of fibrillæ from the cell body of one neuron to other cells; if this can be considered to be of general occurrence, as many histologists believe, the neuron theory, in its original conception at least, would not be tenable. There are, however, so many excellent physiological and anatomical data in its support that we must retain it as the most acceptable theory we at present possess. It might be thought that synapses would transmit impulses with equal readiness in either direction; this is, however, not the case.

The **"valvular" action of synapses.**—If the posterior root of a spinal nerve be divided, and the central end stimulated by an induction shock, it is found that the muscles of the corresponding limb contract; the stimulus apparently passes into the spinal cord and excites the anterior multipolar nerve-cells in the ventral horn of the grey matter, from which the anterior or motor nerve-roots take their origin. It has also been shown by Gotch, Horsely and others, by means of the capillary electrometer, that stimuli pass up the great conducting tracts towards the brain, &c. If the shock be applied, however, to the anterior or efferent root instead of the posterior, no stimuli appear to pass either up the cord or through it to the posterior root, so that the synapse must allow of the passage of the stimuli in the one direction only.

Varieties of Neurons.

The various nerve units which make up the central nervous system differ very considerably in their general characters, such as the form of the parent cell, and the size, number and type of its processes. In some types, such as the pyramidal cells of the cerebral cortex, the axon is very much longer than the dendrites, while in others, belonging to Golgi's second type, the axon is short and forms an arborescence near the cell body.

In the systematic study of the neuron we must consider the character and structure of both the cell body and its processes in some detail.

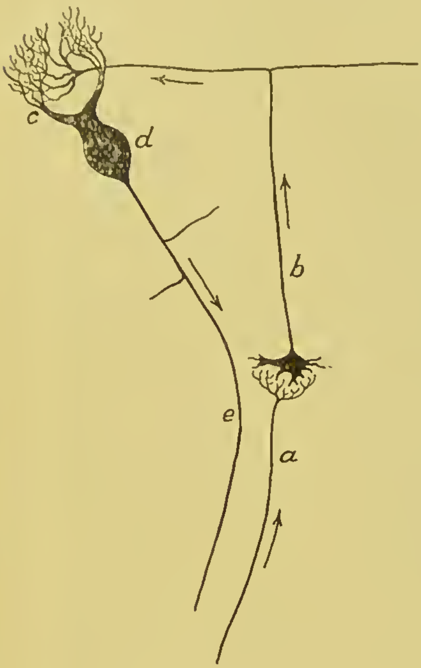

Fig. 390.—DIAGRAM ILLUSTRATING THE "NEURON" THEORY.

The scheme is taken from the cerebellum. An impulse passing up the afferent fibre *a* stimulates through its terminal arborescence the intermediary cell *b*, which in its turn transmits the impulse through the synapse *c* to the antler cell *d*; the energy excited in the cell is then passed down through the axon *e* towards the periphery.

Fig. 391.—CELLS OF GOLGI'S FIRST TYPE.

a, cell; *b*, apical dendron; *c*, lateral dendrites; *d*, axon; *e*, white sheath of collaterals.

The **nerve-cell.**—In its earliest stage of development the nerve-cell is rounded or ovoid and possesses a power of amœboid movement which carries it to its position in the central nervous system; it then becomes fixed and throws out processes which may ultimately give the cell a very characteristic appearance, such as we associate with the antler cell of Purkinje, the pyramidal cell of the cerebrum, or the multipolar cell in the ventral horn of the spinal cord. The size may vary within wide limits—between 5 and 50 μ. As the majority of the more characteristic types

have been already discussed in the section dealing with the "Histology of Nerve," we shall merely consider here the structural peculiarities of nerve-cells in general. As a rule, the nerve-cell is an ordinary encapsulated mass of protoplasm with a well formed nucleus containing one or more nucleoli, and exhibiting the ordinary spongioplasmic reticulum, though this is to a great extent obscured by the presence of a second or fibrillary network, which has been the subject of much controversy. It was at one time believed that it was a mere modification of the ordinary spongioplasm, probably by an elongation of its meshes, but the researches of Apathy on the neurons of annelids have definitely proved that the fibrillar is quite distinct from the spongioplasmic reticulum, and that it is directly continuous with the fibrillæ found in the processes leaving the cell. Golgi has corroborated Apathy's researches, by demonstrating the existence of similar independent fibrillary reticula in the ganglion cells of mammals.

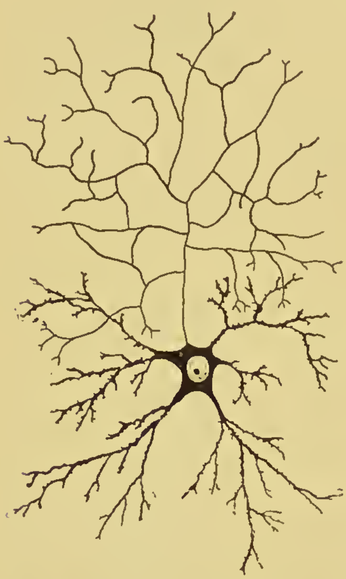

Fig. 392.—Cells of Golgi's Second Type.

In 1892 Nissl and Marinesco described in nerve-cells a peculiar substance which stains very deeply with certain hot aniline dyes, such as methylene or toluidin blue, and which is consequently called the tigroid or chromophyllic substance. It is generally found between the fibrillæ in the form of small lozenge-shaped granules, the arrangement and character of which seems to depend somewhat on the nature and functional condition of the protoplasm. The chemical nature of the granules has been only partially determined; Macallum has shown that a considerable amount of iron is present, and they also seem to contain some nucleo-proteids.

Many physiologists hold that these granules represent some form of food material or energising substance, and, as we shall see presently, there is a considerable amount of evidence in support of this view; in the first place, prolonged activity of the cell leads to a marked reduction in their numbers and to an equally marked change in their appearance and their reaction to stains, while, secondly, they seem to be regenerated during rest.

Of course it must be remembered that the granular appearance, &c., might possibly be due to the methods of fixation which have been employed in the preparation of the section, or are, in other words, artifacts; still, if the same technique be employed in every instance this objection must become somewhat invalidated, for though we may have no exact knowledge of the precise significance of the results obtained, still we are able to recognise those cells which depart materially from the standard appearance which we have learned to attribute to a normal nerve-cell.

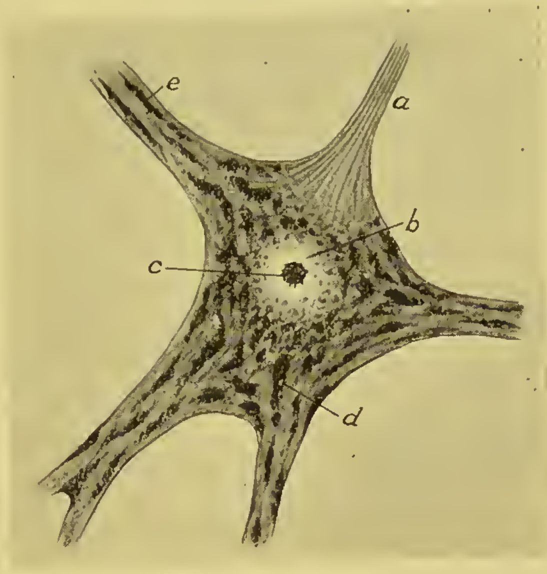

Fig. 393.—Multipolar Nerve-Cell.
a, axon; *b*, nucleus; *c*, nucleolus; *d*, chromatophyllic granules; *e*, dendron.

The chief conditions which seem to affect the nerve-cell, and more especially the chromophyllic substance, are:—Fatigue, prolonged inactivity, interference with the normal supply of the blood and the presence of poisonous materials in the blood (such as the toxins of certain fevers), or chemical agents (such as drugs).

Fatigue.—Gustav Mann and others have demonstrated that in fatigue the most characteristic changes to be noticed are:—(1) A primary swelling followed by a diminution in the size of the nucleus; (2) a shrinkage of the cellular protoplasm, and in very marked instances vacuolation; (3) a very distinct reduction in the amount of the chromophyllic material and a change in the appearance of the granules—they lose their lozenge shape and become somewhat fusiform, while the staining becomes very diffuse; (4) the cell as a whole becomes smaller, and in prolonged fatigue may materially alter in shape.

A series of experiments carried out by Hodge also shows very clearly the chief changes which occur in fatigue, more especially in the nucleus and cytoplasm. Hodge stimulated a mixed nerve for some time by means of an interrupted current, and then removed and fixed the corresponding spinal ganglia, employing

some of the other ganglia as contrasts. The stimuli were of varying duration, from fifteen to thirty seconds every minute for some hours; he found that changes took place in every part of the cell. The nucleus became much smaller and frequently changed its position in the cytoplasm. The diminution in size appeared also to be proportionate to the duration of the stimulation; he estimated the shrinkage to be about 22 per cent. of its volume at the end of one hour, 24 per cent. after five hours, and 44 per cent. after ten hours. He also found that complete recovery had taken place after a lapse of twenty-four hours.

Arrested activity also produces characteristic changes in the cell, and more especially in the chromophyllic material. If the anterior nerve-root of a spinal nerve be divided, so that the cells in the ventral horn, which send their axonic processes into the root, are rendered functionless, degeneration in the granules at once takes place. They diminish in size, lose their angular outlines, and ultimately either disappear entirely or are reduced to a non-granular condition. This degenerative process is called *chromatolysis.*

The cell body may primarily be slightly swollen, but soon becomes smaller, and in certain cases may entirely atrophy. The process generally begins within twenty-four hours of the establishment of the lesion, and may continue for several weeks; it appears to spread from the attachment of the axon through the body of the cell to the dendrites. The extent to which repair can take place is as yet undetermined. There is much evidence to show that in motor cells at least very considerable if not complete repair can take place, even though the axon be permanently destroyed; in this instance it must be supposed that the energy generated in the cell finds an outlet by some fresh path. Section of the posterior nerve-root does not seem to produce any very marked chromatolysis in the cells of the corresponding spinal ganglion, though this does not seem to be the case with all forms of sensory cells, for von Gehuchten has pointed out that section of the pneumogastric produces well-marked changes in the ganglion of the nerve, and that they seem to possess little or no power of recovery. Schäfer has also found complete and permanent chromatolysis in the cells of Clarke's column after division of the postero-lateral cerebellar tract of the cord.

The degenerative change need not result from a direct extension of the process from the axon to the body of the cell, for Warrington has shown that the cells of the ventral horn undergo chromatolysis after section of the posterior nerve-roots. As there is no continuity between these cells and the fibres of the posterior root,

the degeneration can only result from the failure of sensory impulses to reach and thereby to stimulate the cells.

Interference with the blood supply to the area, as by ligature of the artery, produces complete chromatolysis; the same result is found to follow after the administration of large quantities of certain *drugs*, such as cocaine or strychnine, as well as in some toxæmic states of the blood, as in rabies, tetanus, &c.

It may therefore be concluded that the physiological condition of a nerve-cell depends essentially on two factors, viz., the presence of an adequate supply of healthy blood, and the reception or transmission of nervous impulses; that any interference with either factor induces degenerative or chromatolytic changes in the cell; and, finally, that the severity and the permanence of these changes depend on the nature and extent of the condition causing them.

Growth of the neuron.—The axon is generally extruded from the cell prior to the dendrites, and is at first a very short and slender process; as the cell becomes older, the fibre necessarily increases both in length and in thickness and ultimately develops a medullary or white sheath. The dendrites are at first few in number and short, and their development is somewhat slower than that of the axon, for we may find the latter practically fully formed while the dendrites are as yet immature. Indeed, it probably takes many years before they are fully formed. Concomitantly with the growth of the cell, there is a condensation of the protoplasm and a development of the tigroid material.

Fig. 394.—Scheme of the Development of a Neuron.

The axon is the first to develop.

In old age, on the other hand, there seems to be a retrogressive change; the cell becomes smaller, the nucleus shrinks and the tigroid substance less abundant. Not infrequently the nucleus entirely disappears, a point of considerable interest, as it is peculiarly well developed in the majority of nerve-cells. Finally, the processes, and more especially the dendrites, diminish in size.

Cell processes.—It has been already mentioned that nerve-cells possess two types of processes—the axonic and the dendritic—and we must now consider these in greater detail. The axon, which is generally single, leaves the cell at a somewhat oval swelling or nerve hillock, which is singularly free from Nissl's granules but is prominently fibrillated. The process is generally slender and of almost uniform thickness throughout its length. The length of the axon varies greatly with the type of cell; in those belonging to Golgi's first class, such as the pyramidal cells of the cerebral cortex, it is of great length when fully developed, as it extends from the surface layers of the brain practically throughout the whole of the nervous system down to the lum-

Fig. 395.—Cells of Golgi's First Type.

a, cell; *b*, apical dendron; *c*, lateral dendrites; *d*, axon; *e*, white sheath of collaterals.

Fig. 396.—Cells of Golgi's Second Type.

bar region of the spinal cord, a distance of from 45 to 60 centimetres. In the cells of Golgi's second class, on the contrary, the axon is quite short, and may break up into its terminal arborescence in the immediate vicinity of the parent cell. At a short distance

from its origin the fibril gives off a number of collatcrals which pass away, generally at right angles, into the surrounding tissue.

The dendrites leave the cell by thick rootlets containing numerous granules; they soon divide into a large number of branches which sub-divide again and again, so that a more or less complex arborescence is ultimately formed. This is especially evident in certain cells, such as the antler or Purkinje cells in the cerebellum.

While the majority of nerve-cells show these two types of processes, a certain number are found which have either a single fibre or two identical in character. These forms are especially numerous in the developing spinal ganglion, where a process may be seen leaving each pole of the ovoid ganglion cell; as development proceeds the two blend so that the cell apparently possesses a single process, which later bifurcates. In this instance we have apparently a double axon.

Functions of the processes.—Leaving out of consideration the original theory, now untenable, that the dendrites, like the rootlets of plants, supply the cell with nourishment, we must consider whether the different processes have independent functions or whether they can transmit impulses in either direction to the cell body. It is most probable that the axon conveys impulses *from* the cell to the tissues, and is therefore centrifugal, while the dendrites transmit impulses derived from synapses with other fibres *to* the cell, and are therefore centripetal. This "law of axipetal conduction" is probably applicable to the great majority of nerve-cells, though it certainly cannot be applied to those of the bipolar type, as in the spinal ganglia, where the one axon must necessarily be centripetal and the other centrifugal.

Classification of Nerve-Cells.

There are two methods of classification commonly employed, one based on the morphology of the various cells, such as unipolar, bipolar, multipolar, antler, pyramidal, &c., and the other on their probable function. Professor Schäfer classifies them into four groups, viz., afferent, efferent, intermediate and distributing.

Afferent or receptive cells.—These receive impressions from the periphery and transmit them to the central nervous system. The cells of the spinal ganglia are excellent examples of this class, and it will be remembered that such cells are originally, as in the earthworm, situated at the periphery, and are connected with the central nervous system by a fibre or process; as we ascend in the

animal scale, the cell sinks below the surface, to which it remains connected by a peripheral process representing a sensory nerve-fibre. The olfactory cells of vertebrates afford an example of a primitive condition which has persisted in a higher type.

Efferent cells.—These send out nervous impulses to the periphery, *e.g.*, the cells in the anterior horn of the cord or the pyramidal cells of the cerebrum. Both afferent and efferent cells are often called root-cells.

Intermediary cells.—These receive impressions from afferent cells and transmit them, directly or indirectly, to the cells of the efferent group.

Distributing cells.—These are chiefly found in the sympathetic chain and its collateral ganglia and apparently transmit impulses more especially to involuntary muscle fibres and secreting glands.

The Neuroglia or Supporting Tissue of the Nervous System.

The neuroglia which forms the supporting tissue of both the grey and the white matter consists of a felted network of interlacing but non-branching fibrils which inter-penetrate the nervous elements and support them. It is not, however, ordinary connective tissue, as it is epiblastic and not mesoblastic in formation, and as its chief constituent is " neurokeratin," a substance which gives most of the ordinary reactions of proteid but is insoluble in the ordinary digestive juices, and which contains a high percentage of sulphur in its molecules. It is derived from the spongioblasts of the primitive neural tube, which at first form a continuous lining to the canal, and later throw out processes into the surrounding nervous matter. As the central nervous system develops, many of the cells wander into its substance and acquire processes which pass in all directions, forming a fibrillary entanglement around the developing nerve-fibres. Though this undoubtedly seems to be a mode of origin of many of the neuroglia cells and their fibres, still in the adult the interlacing fibres can be seen by a special method of Weigert to be independent of the cells. This is not confirmed, however, by specimens stained by Golgi's process, where the fibres seem to spring from the reduced bodies of the glia cells. For the most part, the neuroglial network seems to be more dense in the grey matter than in the white, although even in the latter it practically separates each nerve-fibre from its neighbour. It is especially in evidence around the central canal of the spinal cord and around the ventricles of the brain, and mingled with small nerve-cells it forms a cap to the posterior horn of grey matter,

called the substantia gelatinosa of Rolando. There is considerable doubt, however, as to the accuracy of this statement.

Spinal Cord.

The spinal cord is enclosed within three membranes, called the dura mater, pia mater, and arachnoid mater respectively.

The outermost membrane, or dura mater, surrounds the cord loosely and is attached to the bodies of the vertebræ in front, and also to the spinal nerves, which it supplies with connective tissue sheaths. It consists of dense fibrous tissue, and is entirely protective in function.

The arachnoid mater, unlike the dura, is an extremely delicate membrane; it is arranged in two layers, one of which lines the inner aspect of the dura and is practically incorporated with it, while the other is separated from the pia mater by a lymphatic space, crossed by bands of delicate connective tissue.

The third membrane, or pia mater, invests the spinal cord and sends fibrous trabeculæ and blood-vessels into its substance.

Structure of the Spinal Cord.—The cord is composed of two lateral halves, joined by a central band of nervous tissue called the isthmus. The separation is effected by the presence of two fissures, of which the anterior, though shallow, is broad, and therefore very distinct (Fig. 397, *a*). The posterior can hardly be considered a true fissure, as it is formed by the presence of a connective tissue septum derived from the pial investment. Each lateral half shows an external zone of a pearly-white colour, and consequently called the white matter, surrounding an inner comma-shaped mass of a pinky-grey tint. The isthmus consists partly of white and partly of grey matter; the former lies immediately behind the anterior fissure (*q*) and is called the anterior or white commissure, while the grey or posterior commissure which unites the grey crescents is further divided into two portions, the one lying in front of the central canal of the cord and the other behind.

The **grey matter.**—Each lateral mass is of a somewhat crescentic shape, with its concavity directed outwards. Anteriorly, it shows a well-marked swelling, called the anterior or ventral horn (*m*), containing numerous nerve-cells, while posteriorly it is somewhat pointed, and terminates in a mass of neuroglia called the substantia gelatinosa of Rolando. As the substantia forms a rounded end to the horn it is frequently called the caput. In the

dorsal region of the cord there is a third or lateral cornu which projects outwards from the concavity of the crescent into the white matter. Both the anterior and the posterior cornua give origin to nerve-fibres which pass outwards through the white substance and emerge from the cord as the anterior and the posterior nerve-roots respectively. The anterior (*h*) root leaves the ventral

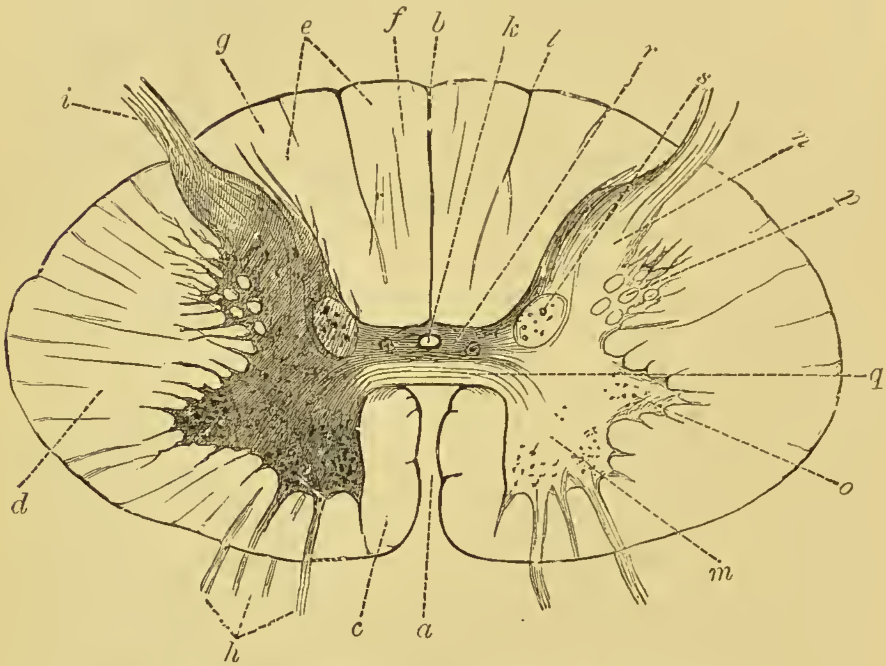

Fig. 397.—Transverse Section of Human Spinal Cord.

horn in a series of separate nerve-bundles which unite later; the posterior (*i*), on the other hand, forms a single well-marked fasciculus running between the caput and the surface of the cord. The passage of these bundles of fibres through the white matter divides the latter into two segments, namely, a posterior between the dorsal fissure and the posterior nerve-root fibres, and an antero-lateral extending from the same root behind to the antero-mesial fissure in front.

Structure of the white matter.—The white matter consists of medullated nerve-fibres running longitudinally in the cord, which are enclosed in a reticulum of neuroglia, composed of small irregular glia-cells with well-marked processes. As the fibres pass down the cord they give off collaterals, which pass into the grey

matter at various levels and form synapses with cells there. The fibres vary greatly in diameter and are medullated.

Structure of the grey matter.—It consists principally of vast numbers of nerve-fibrillæ, mainly non-medullated, which are also imbedded in a reticular framework of supporting neuroglia. In addition, we have a number of nerve-cells of various shapes and sizes, but it must be remembered that the fibrillary element greatly predominates.

The fibres are derived from many sources, of which the following are perhaps the most important. A certain number are the axonic and dendritic processes of the cells in the grey matter itself; a second set of fibres of small diameter are apparently collaterals derived from the longitudinal fibres in the white matter, while the rest ramify in the grey matter itself, and are probably commissural in character.

Arrangement of the nerve-cells in the grey matter.—In the ventral horn we have several groups of large nerve-cells with many processes, and consequently called the anterior multipolar nerve-cells. Though found at all levels in the cord, they are especially in evidence in the cervical and lumbar segments, where the nerve-roots which go to make up the cervical, brachial and lumbar plexuses are given off. They are also found in increased numbers at the level of emergence of each nerve-root. The cells of the ventral horn are arranged in groups, of these two are of especial importance, one lying close to the mass of white matter bounding the anterior fissure, and called the median or internal group; while the second, occupying the outer and posterior part of the same horn, is frequently subdivided into several small collections of cells named, according to their position in the horn, as antero-lateral, postero-lateral, &c.

The structure of the anterior multipolar nerve-cell has been already considered (page 143), but it must be carefully remembered that their axonic processes pass out into the anterior nerve-roots, while the dendrites arborise in the surrounding grey matter. In the posterior horn we find at all levels in the cord a considerable number of cells, somewhat smaller than those of the ventral cornu. Generally speaking, the cells are massed in two groups, one lying on each side of the horn. As the cells lie in a network formed by the fibres of the posterior nerve-root, they are often called the cells of the posterior reticular formation. Their axons apparently pass into the grey matter, and probably end chiefly in the ventral horn in synapses with the anterior multipolar nerve-cells. In addition to these two groups we find other collections of small cells, some

in the substantia gelatinosa of Rolando, and others irregularly scattered among the fibres entering the posterior horn.

At the junction of the posterior horn with the grey commissure lies a very well marked group of cells of peculiar importance, on account of their size and their probable connections. These cells form a very distinct tract, called the vesicular column of Clarke, extending from the level of the lower cervical segments above to the third lumbar segment below; it is extremely well developed in the dorsal region, where it forms the dorsal nucleus of Stilling. Beyond the levels we have mentioned, the cells do not form a continuous chain, but are found in scattered groups, forming the so-called cervical and lumbar nuclei. The posterior vesicular column of Clarke is composed of large multipolar cells which send their axons into the lateral columns of the white matter (tracts of Flechsig and Gowers). The cells lie somewhat obliquely, so that in ordinary transverse sections of the spinal cord they appear smaller than they really are. They are fusiform in shape and may measure from 40 to 90 μ (Mott). The whole column of cells is surrounded by a mass of delicate fibrillæ apparently derived from the posterior root fibres as they pass into and up the posterior root zone.

In the cervical region more especially, a group of cells can be seen about the middle of the concavity of the grey matter, called the crescent cells. Also in the thoracic region, where there is a third or lateral horn, a number of multipolar cells are present, somewhat similar to those of the ventral cornu but smaller in size.

Differentiation of the white matter into tracts.—The white matter, under ordinary conditions, is not differentiated into any tracts or columns, except in the posterior segment, where a septum of fibrous tissue divides it into postero-external and postero-internal zones, commonly called the tracts of Burdach and Goll. By the employment, however, of special methods of research, we are enabled to map out the white matter into definite areas, which contain bands of fibres which pass in certain directions and are generally designated tracts.

It will be remembered that Waller, in a series of experiments on the spinal nerve-roots, proved that the separation of a nerve-fibre from its parent cell was always followed by a degeneration of certain portions of the nerve, viz., the axon and the medullary sheath; and it is on the basis of this great discovery that our knowledge of the paths pursued by the various fibres which lie in the white matter chiefly rests.

It will also be recollected that the medullary substance degenerates into a fatty or oily material which stains an intense

black with osmic acid, while the axon completely disappears. After the degeneration has been fully established, the oily substance beeomes gradually removed, so that the tissue no longer stains with the reagent.

The neurilemmar changes—such as repeated division of the nuclei—whieh are generally well marked in lesions of the peripheral nerves, are not demonstrable in the spinal cord, as the fibres do not possess a grey sheath. The degeneration may be induced either by section of some of the posterior nerve-roots, which send their fibres into and up its substanee, or by aetual division of the eord itself. It will then be found that eertain areas of the white matter *above* the line of lesion show degeneration (tracts of ascending degeneration); while other portions are similarly affected below that level (traets of descending degeneration).

The signifieanee of these phenomena is suffieiently obvious; the paths of aseending degeneration must contain fibres which have their trophic eells situated at a lower level in the cord, or in the ganglia on the posterior nerve-roots; while in the case of the tracts of descending degeneration the trophie eells must lie above the line of the lesion. It must be clearly understood, however, that the terms ascending and deseending do not apply to the functional nature of the tract, though in the majority of instanees it does happen that the deseending traets convey impulses down the cord and *vice versa*. The degenerated traets ean be differentiated in several ways.

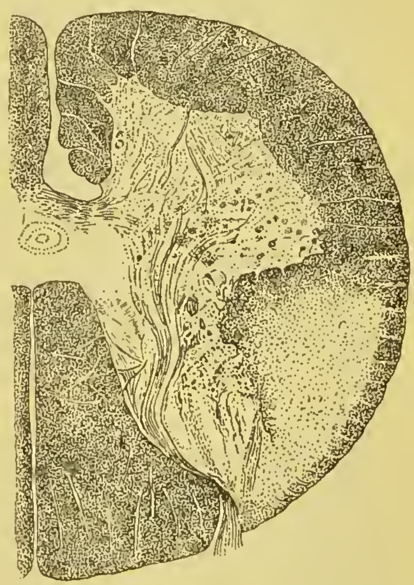

Fig. 398.—Transverse Section of Cord (Weigert's Method).

Treated by Weigert's process, for instanee, the area in whieh the nerve-fibres have completely broken down can be recognised by its inability to take the stain. If, however, it be desired to demonstrate the presence of isolated *degenerating* fibres in the midst of normal ones—and this is frequently the case—Weigert's method is insufficient for the purpose; it is, indeed, only suitable when the fibres have degenerated to some extent *en masse*.

Marchi's method is invaluable in the detection of isolated *degenerating* fibres. It depends on the fact, which we have already mentioned, that the medullary sheath in breaking up into an oily substance stains like ordinary fat. The method is applicable only during the process of degeneration, *i.e.,* during the first few weeks subsequent to the lesion and not after the nervous matter has been completely replaced by neuroglia, when Weigert's method is adopted.

The technique of Marchi's method may be summarised as follows:—

The tissue is placed in Müller's fluid for about a fortnight, and subsequently in a mixture of osmic acid and Müller's fluid.

The normal medullary sheaths are unaffected by the osmic acid, while the degenerating fibres are blackened in the usual way.

The various tracts in the white matter can also be ascertained by noting the period at which the constituent fibres acquire their medullary sheaths.

The sensory or centripetal tracts are alone medullated during fœtal life. It is first apparent in the columns in the posterior columns of the cord (Goll and Burdach) and at a later period in the lateral ascending cerebellar tracts (Flechsig and Gowers).

The efferent or motor columns are not medullated until after birth. The accompanying figure stained by Weigert's method illustrates the appearance of a transverse section of the cord in a new-born child. (Fig. 398).

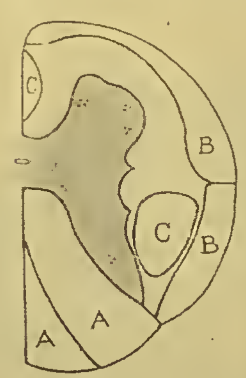

Fig. 399.—Diagram Illustrating the Periods of Medullation in the Cord.

A, A, the posterior columns of Goll and Burdach; B, B, the lateral cerebellar tracts of Flechsig and Gowers; C, C, the descending pyramidal tracts which medullate at or after birth.

Tracts of ascending degeneration.—If sections be made above and below the level of a transverse lesion of the spinal cord, say in the mid-dorsal region, it will be found that the areas of degeneration differ in the two instances. In sections taken through segments *above* the lesion, the following tracts can be seen.

1. and 2. *The posterior columns of Goll and Burdach.*—A

very large area lying between the posterior nerve-roots and the postero-median fissure, which is divided into two portions, an external, or column of Burdach, and an internal, or column of Goll, by the presence of a delicate connective tissue septum. Both tracts become larger as they pass upwards through the cord, and contain fibres which pass into two nuclear swellings on the posterior aspect of the medulla, called the nuclei cuncatus and gracilis. The fibres are derived from the inner bundle of the posterior root fibres of the spinal nerves.

3. and 4. *The lateral ascending cerebellar ascending tracts of Flechsig and Gowers.*—In the antero-lateral region of the white matter lies a peripheral, somewhat comma-shaped area—the ascending tract of Gowers. The origin of the fibres contained in the column is somewhat doubtful. Many are certainly the axonic processes of the cells of Clarke's column, while others seem to be derived from cells situated in the lateral and posterior portions of the ventral horn. The tract is found in all parts of the cord, and, as we will see later, the fibres pass indirectly to the grey matter of the cerebellar cortex. The *postero-lateral ascending cerebellar* tract of Flechsig is directly continuous posteriorly with the column of Gowers, and is composed of fibres which appear to rise from the cells of Clarke's vesicular column and from cells in the posterior horn. Like the fibres in Gowers' tract, they pass upwards throughout the length of the cord, and terminate in synapses in the cerebellar cortex. The two sets of fibres enter the cerebellum, however, by different routes, as the tract of Flechsig becomes incorporated with the inferior peduncle, while that of Gowers passes upwards primarily into the mid brain and later through the superior peduncle into the cerebellum.

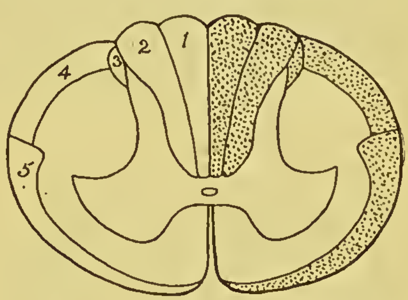

Fig. 400.—Scheme of the Ascending Tracts in the White Matter.

1, Postero-internal (column of Goll); 2, postero-external (column of Burdach); 3, marginal (Lissauer); 4, postero-lateral ascending cerebellar (Flechsig); 5, antero-lateral ascending cerebellar (Gowers).

5. *Tract of Lissauer.*—This is a very small area lying almost immediately external to the posterior roots as they pass through the white matter to enter the posterior cornu. The fibres are derived from the outer bundle of the posterior root-fibres and pass later into the grey matter of the posterior horn at higher levels, and into the posterior white columns. All these tracts, except the

2 x

last, run upwards throughout the whole length of the cord, and are consequently called the "long ascending."

Tracts of descending degeneration.—If we next examine a section of the cord taken through a segment *below* the lesion, we will find that a completely different set of areas have undergone degeneration. Of these the most important probably are :—

1. and 2. *The pyramidal tracts of Türck.*—In man and in some of the higher apes there are two pyramidal tracts, called the direct and the crossed respectively.

The *direct pyramidal* tract is a mass of white matter lying immediately external to the anterior fissure, and is composed of fibres which take origin in the Rolandic areas of the cerebral cortex. As we shall see later, these descending motor fibres on reaching the medulla divide into two bands, one of which decussates to pass down in the crossed pyramidal tract of the cord, while the remaining and smaller fasciculus does not cross, but passes down the cord in this direct tract. The column is of small size and is only found in the cervical and upper dorsal regions, as it diminishes rapidly in volume as it passes down the cord, from the passage of the fibres through the anterior or white commissure to the ventral horn of the other side.

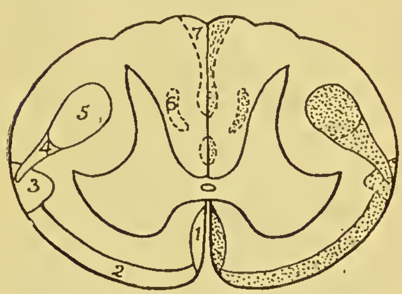

Fig. 401.—Scheme of the Descending Tracts in the White Matter.

1, Direct pyramidal (Türck); 2, descending cerebellar or vestibulo-spinal (Löwenthal); 3, tract of Helweg; 4, pre-pyramidal or rubro-spinal (Monakow); 5, crossed pyramidal (Türck); 6, comma tract; 7, association tracts, containing both ascending and descending fibres.

The *crossed pyramidal* is one of the most constant tracts in the spinal cord, though it varies very considerably in position in the different animals ; in rodents it is situated in the posterior segment of the cord, whilst in some others it lies close to or even among the fibres of the posterior nerve-roots. In man the fasciculus is very well developed, and is found immediately internal to the postero-lateral ascending tract of Flechsig in the upper part of the cord ; in the lower segments of the cord, however, the tract lies nearer the surface. The position, &c., of the tract can be readily determined by destroying the Rolandic areas on one side of the cerebrum, so as to induce degeneration of the descending fibres. Fig. 402 demonstrates the degenerative changes which follow a lesion of this type. The tract, as we should naturally expect, is

largest in the upper portion of the cord, as fibres pass from it at all levels to enter the white matter, where they form synapses with cells, more especially in the posterior horn (Schäfer).

3. *The pre-pyramidal tract of Monakow, or rubro-spinal tract* (*Schäfer*).—This is a small tract lying antero-external to the crossed pyramidal. It seems to consist of fibres which take origin in the red nucleus of the crus; and which terminate in synapses with the cells in the crescent.

4. *The descending cerebellar tract of Löwenthal.*—The fibres may either be arranged in small and somewhat scattered fasciculi among the fibres of the antero-lateral ascending tract of Gowers, or they may be collected into a fairly distinct column immediately internal to

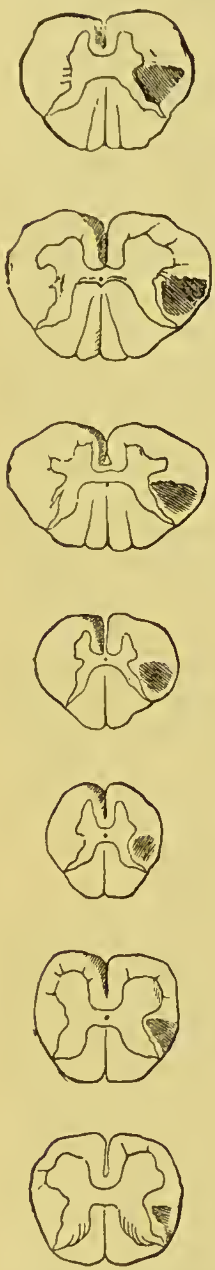

Fig. 402.—Secondary Descending Degeneration following a Lesion of the Left Cerebral Hemisphere.

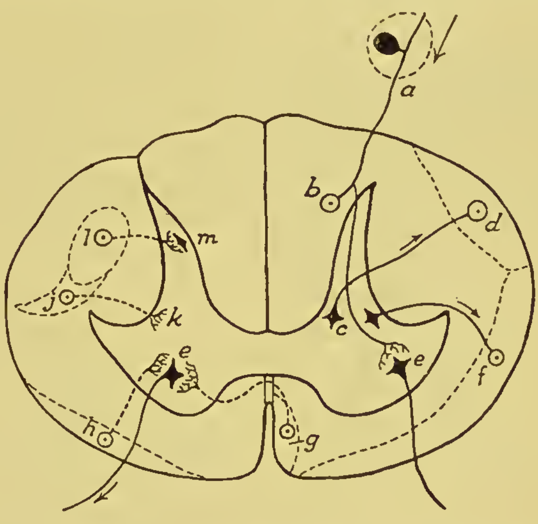

Fig. 403.—Scheme Illustrating the probable Connections of the Long Fibres of the Tracts with the Cells in the Grey Matter.

On the left side of diagram we have the descending fibres, viz.:—*h*, descending cerebellar fibres passing to synapses in the ventral horn, *e*; *i*, crossed pyramidal fibres synapsing with the post-cornual cells, *m*; *j*, pre-pyramidal fibres passing to cells in the crescent, *k*. On the right we have the posterior root-fibres, *a*, passing into the cord and forming synapses with the ventral cells, *e*, and the cells of Clarke's column, *c*; also axons passing from Clarke's cells into the posterior ascending cerebellar tract of Flechsig, *d*, and from neighbouring cells into the tract of Gowers, *f*.

it. They are probably derived from groups of cells in the mid-brain, more especially in the corpora quadrigemina and the vestibular (hence it is frequently called the vestibulo-spinal tract) nucleus of Deiters. The fibres are found in the ventral and dorsal longitudinal fasciculi which pass downwards from the tegmental region to the medulla. The fibres do not seem to be derived to any large extent from the cerebellum directly, though they probably have a very distinct functional connection with that organ through Deiter's nucleus. They enter the ventral horn and terminate in synapses with the anterior multipolar cells.

5. *Tract of Helweg.*—A very small and badly-marked fasciculus situated at the periphery of the cord immediately external to the anterior nerve-roots. It is only distinctly seen in the cervical region. The fibres probably come from a group of cells in the medulla near the olivary nucleus.

6. *The comma tract.*—A group of fibres, situated in the postero-external tract (Burdach's column), which come from the posterior root fibres. They pass into the grey matter at lower levels and terminate in synapses with the cells of both the anterior horn and the vesicular column of Clarke.

7. A considerable number of smaller tracts have been described, but they seem to consist almost entirely of commissural fibres.

Fig. 404. — Scheme of the Distribution of the Nerve-Fibres in the Posterior Nerve-root.

a, Fibre passing up posterior column towards medulla, and giving off collateral, *b*, which synapses in the grey matter; *c*, rod-fibre passing directly into the grey matter; *d*, cell of Clarke's vesicular column sending its axon into Flechsig's column.

The Nerve-Roots and their probable connections.

The anterior nerve-roots are chiefly composed of medullated fibres of large size, which are derived from the large multipolar cells of the ventral horn. In addition, the root contains a number of smaller fibres of which the origin is somewhat doubtful. Some of these seem to be derived from other cells in the ventral horn, while others come from the lateral and posterior parts of the grey matter. A few of the fibres reach the anterior nerve-root through the anterior or white commissure and appear to be the axons of the cells of the ventral horn of the other side.

Section of the ventral root induces both degenerative changes in the peripheral portion of the nerve and chromatolysis in the nerve-cells from which the fibres take origin, mainly in the corresponding segment of the cord.

The posterior nerve-roots.—In a well-stained section of the spinal cord it will be observed that the apparently single band of fibres which constitutes the posterior root is really composed of several fasciculi, of which two, and in most areas three are especially evident. They are generally termed the internal, median and external nerve-bundles respectively.

The direction pursued by the fibres in the cord can only be determined by section of the posterior nerve-roots between the cord and the spinal ganglion, so that the fibres are separated from their trophic centres in that ganglion, and consequently undergo degeneration. Transverse sections are then made at various levels through the cord, opposite to and above the line of entrance of the affected root fibres, when a series of specimens is obtained which show the direction pursued by the various fibres which have comprised the selected posterior nerve-root. Let us suppose, for instance, that the lower two thoracic and the upper two lumbar dorsal nerve-roots have been divided some days previously, and that sections have been made through the cord at the levels of the tenth thoracic, second thoracic and the fourth cervical segments. In the first (A) the degeneration will be found situated immediately around the posterior horn, and chiefly on its inner aspect, in the tract of Burdach, though Lissauer's tract also shows

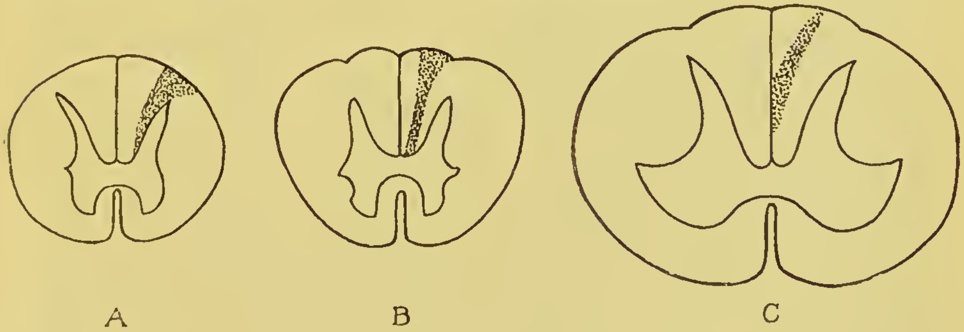

Fig. 405.

degenerative changes. In the second section (B) a well-marked area will be seen not only in the column of Burdach, as in the previous instance, but also in the postero-internal column of Goll, a distinct zone of healthy tissue intervening between the posterior

horn and the patch of degeneration. In the third (C) the area of degeneration is still nearer the middle line and lies entirely in the postero-internal tract of Goll.

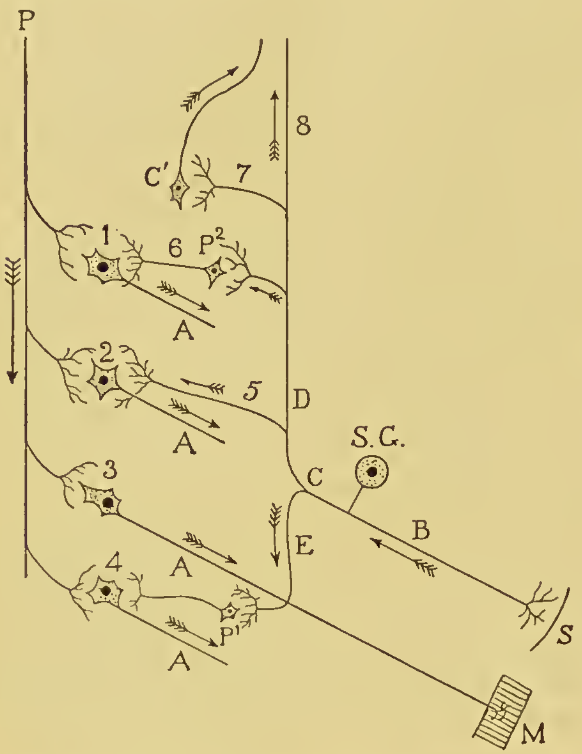

Fig. 406.—Connections of Nerve-Fibres in Spinal Cord.

1,2,3,4, Cells of anterior horn; *A*, axis-cylinder processes given off from them, one of which is shown passing to muscle *M*; *P*, pyramidal tract from which fibres pass, which end in arborisations round 1,2,3,4; *S.G.*, spinal ganglion giving off process which bifurcates into *B*, passing to periphery and skin *S*; and into *C* which passes into the spinal cord, and there itself bifurcates—the branch *E* passing downwards and arborising round one of the cells (p^1) of the posterior cornu, which in turn gives rise to a new axis-cylinder arborising round one of the cells of the anterior horn. The other main branch passes up in the posterior column—some collaterals (5) end by arborising round the cells of the anterior horn; others do so indirectly, first arborising round a cell of the posterior horn (p^2); others terminate round the cells of Clark's column (C^1), and from these cells new axis-cylinders proceed in the direct cerebellar tract to the cerebellum. The main fibre (8) may terminate in any of these ways, higher on the cord or above the cord in the medulla by arborising round a cell of the gracili or cuneate nucleus.

It will be observed also that the size of the degenerated area has considerably diminished in each instance and that Lissauer's tract is only affected in the first set of sections.

From this evidence it would appear that the bulk of the nerve-fibres which pass into the cord by the posterior nerve-roots goes primarily into the postero-external column and later into the column of Goll, up which they run as far as the medulla, where they terminate in synapses with the cells lying in the nucleus gracilis.

The fibres which enter the cord in the upper dorsal and the cervical regions, however, continue to lie in Burdach's column and end in similar synapses in the nucleus cuneatus. While it may be taken as certain that the inner bundle of the posterior root fibres follow this route, there is considerable doubt as to the course pursued by

the fibres in the outer and the middle bundles. The middle ones seem to pass directly into the posterior horn of the grey matter, through the substantia gelatinosa of Rolando, and to enter into synapses with the cells in the posterior horn itself and also with the cells in the column of Clarke. Collaterals are given off from the fibres in bundles, which pass into the grey matter and arborise with the multipolar nerve-cells in the ventral horn and with the cells of Clarke. The outer fasciculus of the posterior root fibres passes primarily into the tract of Lissauer and later into the posterior columns and the posterior horn of the grey matter. All the fibres comprising the posterior root do not, however, pass upwards in the cord; a certain number enter the little comma tract in the postero-external column; they seem to pass downwards in the comma for a short distance only, when they pass into the grey matter and enter into synapses, both in the ventral and the dorsal horns. Finally, as the fibres pass up the cord in the posterior columns they give off at all levels collaterals which end in a similar fashion in the grey matter.

The Medulla Oblongata.

The medulla oblongata or bulb is structurally somewhat complex, as it is the area in which the majority of the nerve-fibres that pass between the brain or cerebellum above and the cord below become arranged, so as to enter into and form the various tracts of the spinal cord which have already been described. It also contains certain masses of grey matter, some of which are intimately connected with the roots of the cranial nerves.

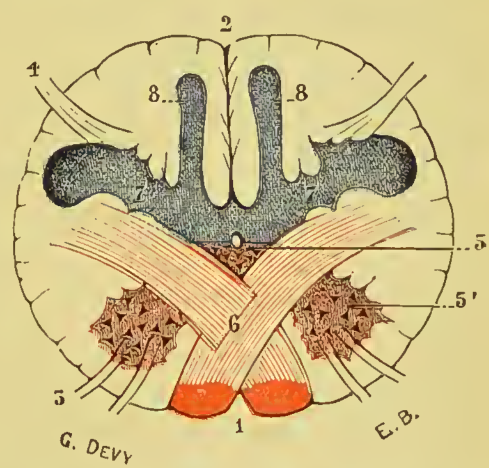

Fig. 407.—DIAGRAMMATIC SECTION THROUGH THE LOWER PART OF THE MEDULLA (AT THE INFERIOR OR MOTOR DECUSSATION) (TESTUT).

1, Antero-median fissure; 2, postero-median fissure; 6, pyramidal decussation; 3, separated anterior cornua; 5, central canal; 7, posterior cornua of grey matter; 8, beginning of the nucleus gracilis.

It is somewhat difficult to obtain an accurate conception of the organ, as the structure varies very considerably in its different parts; thus at its lowest levels the arrangement very closely resembles that of the cord, whilst in the upper part, where the grey matter has been completely broken

up, all this resemblanee is lost and the strueture approximates to that of the pons varolii. The bulb ean be divided into four areas :—(1) The region of the inferior or motor deeussation ; (2) the region of the superior or sensory deeussation ; (3) the region containing the olivary body ; (4) the region immediately above the olive and adjaeent to the pons.

In the first area (Fig. 408), it will be observed that the anterior cornua of the grey matter, whieh are so prominently seen in the spinal cord, are forced outwards by the interposition of bundles of deeussating nerve-fibres, called the decussation of the pyramids. The fibres can be seen in the Fig. passing over to the position oeeupied in the cord by the erossed pyramidal tract. The posterior horn is also rotated outwards and rounded at its extremity. From the root of the dorsal horn of the grey matter a proeess passes backwards into the postero-median eolumn of the white substance, forming the lower portion of the nucleus gracilis. The ventral fissure is small but broad, while the posterior is not changed to any extent.

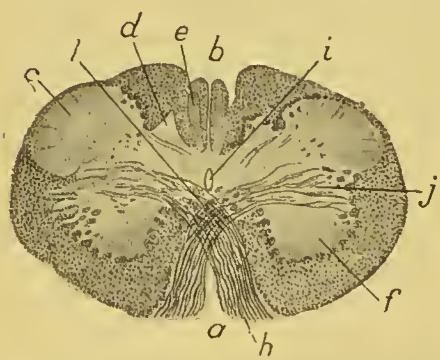

Fig. 408. — Transverse Section of Medulla of Cat at the Level of the Decussation of the Pyramids.

a, Anterior median fissure ; *b*, posterior median fissure ; *c*, caput of posterior horn ; *d*, commencing cuneate nucleus ; *e*, commencing clavate nucleus ; *f*, head of anterior horn becoming isolated ; *h*, fibres of anterior pyramid ; *i*, central canal ; *l*, decussation at bottom of anterior fissure ; *i*, fibres passing across root of anterior horn.

In the second section, taken through the organ in the plane of the superior or sensory decussation, below the olivary body and a little above the last, it will be seen that the arrangement of the grey and the white matter is very eonsiderably altered. At the side of the anterior fissure lie the pyramidal or deseending fibres, forming a well-marked faseieulus, and immediately behind somewhat scattered bundles of vertical fibres—the lemniseus or fillet—which we shall discuss in some detail later. It will also be observed that the anterior cornua have separated from the rest of the grey matter and form independent rounded masses, called the antero-lateral nuclei.

The posterior horn is now represented by a series of three nuelei, two situated in the centre of the swollen terminations of the two posterior columns of the cord, and called the nucleus gracilis and the nucleus cuneatus, whilst the third, or nueleus of

Rolando, lies most external and represents the original caput of the posterior horn; the Rolandic nucleus is capped by the substantia gelatinosa and the descending root of the fifth nerve. The scheme shows also the presence of certain fibres derived from cells in the two posterior nuclei, which cross the middle line and unite later to form the ascending band of the fillet. The intersection of these fibres forms the superior or sensory decussation; it extends as far upwards as the posterior third of the olivary body. (The decussation is represented in Fig. 410 by the letter *l*.) The rest of the grey matter becomes lost in the formatio reticularis, a reticulum formed by the interlacement of longitudinal and transverse fibres among the disassociated elements of the original grey matter, more especially of the ventral horn. It is situated in the antero-lateral portion of the bulb, behind the pyramids and olivary bodies.

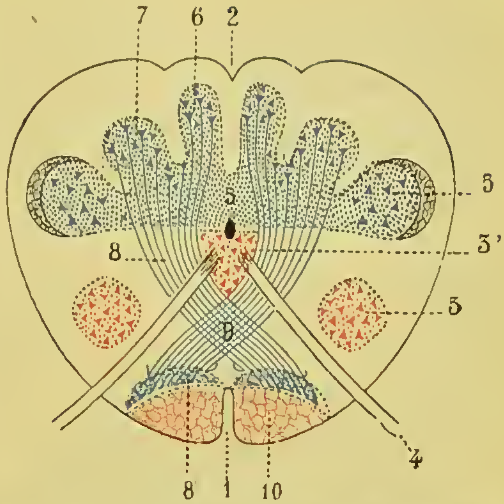

Fig. 409. — Scheme of the Structure of the Medulla at the Level of the Superior or Sensory Decussation (Testut).

1, Anterior fissure; 2, posterior fissure; 3, antero-lateral nucleus; 4, hypoglossal; 5, central canal; 6, nucleus gracilis; 7, nucleus cuneatus; 5, nucleus of Rolando capped by the descending root of the fifth nerve; 8, formatio reticularis.

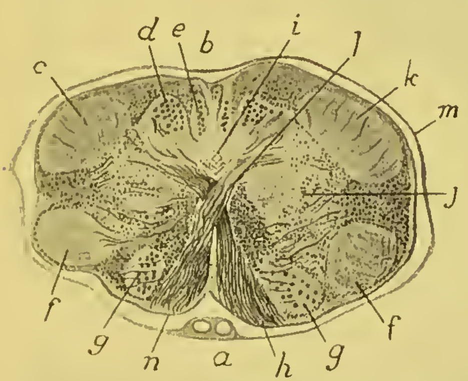

Fig. 410.—Transverse Section of Medulla of Cat at the Level of the Lower Part of the Olive.

a, Anterior median fissure; *b*, posterior median fissure; *c*, *k*, caput of posterior horn; *d*, nucleus cuneatus; *e*, nucleus gracilis (clavate nucleus); *f*, head of anterior horn, separated (nucleus lateralis); *g*, olive; *h*, anterior pyramid; *i*, central canal; *j*, commencement of formatio reticularis; *l*, decussation; *m*, *n*, membranes of the medulla.

The longitudinal fibres are chiefly collected into bands, of which the most important are the lemniscus in front and the posterior longitudinal fasciculus behind. Both of these bands are best marked in the upper part of the bulb, and, as we shall see later, pass upwards into the pons and crus.

The transverse fibres belong to the arcuate system. Of these we have two sets, an external or superficial, and an internal or deep; the internal we have already seen arising from cells in the nucleus gracilis and nucleus cuneatus, and running obliquely forwards across the middle line to join the fibres of the fillet (Fig. 410). The external fibres run a more tortuous course;

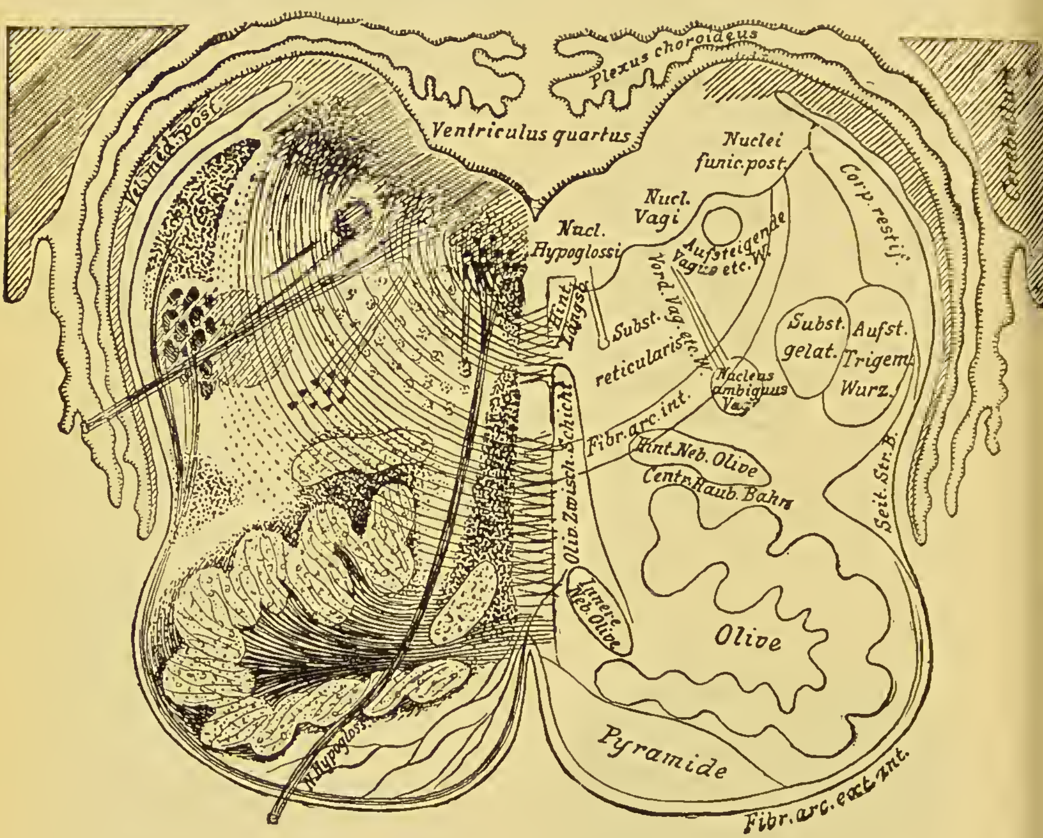

Fig. 411.—Transverse Section of Medulla at about the level of the middle of the Olivary Body.

The names largely indicate the parts shown. On the left are seen two nerves passing into the medulla, the upper of which is the vagus or tenth, while the lower, to the inner side of the olivary body, is the hypoglossal or twelfth. Immediately to the outer side of the nucleus of reception of the vagus is indicated the fasciculus solitarius, by a circle on the right side and by a corresponding shaded portion on the left. The nucleus ambiguus is also shown on both sides, its cells of origin for fibres going to join the vagus being indicated on the left. The student should compare this scheme with the preceding figure.

one band passes out by the anterior fissure from the reticular formation of the other side and sweeps along externally to the pyramids as far as the olivary body, where it is joined by a

second fasciculus that encircles the anterior aspect of that body. The combined fibres form a very distinct band which passes round externally to the Rolandic and cuneate nuclei and becomes incorporated in the restiform body.

In the upper part of the bulb there is a still more marked change in the arrangement of the structural elements. This is partly due to the inclusion of fresh masses of grey matter, such as the olives and the accessory olives, and partly from the widening of the posterior fissure, so that the original central canal of the cord becomes transformed into the fourth ventricle.

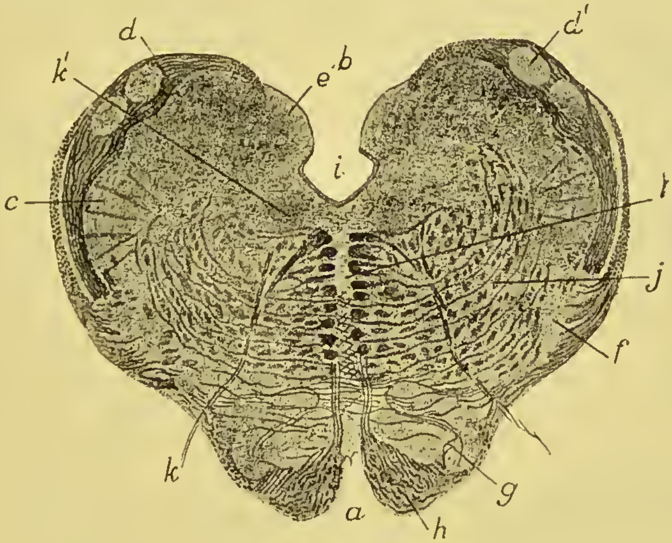

Fig. 412.—Transverse Section of Medulla of Cat at Level of commencement of Fourth Ventricle.

a, Anterior median fissure; *b*, posterior median fissure opening into central canal, *i*; *c*, caput of posterior horn; *d*, cuneate nucleus; *d'*, external cuneate nucleus; *e*, nucleus gracilis; *f*, nucleus lateralis; *g*, olive; *h*, anterior pyramid; *i*, central canal, opening to form floor of fourth ventricle; *j*, formatio reticularis; *k*, spinal accessory nerve; *k'*, nucleus of spinal accessory; *l*, median raphé.

The belt of grey matter immediately anterior to the central canal becomes differentiated to form nuclear masses, the majority of which are connected with the roots of the cranial nerves. In point of fact, some of the cranial nuclei can be seen at a much lower level in the medulla. In the case of the hypoglossal the nuclear origin of the nerve is peculiarly distinct.

At the lower level of the pyramidal decussation the fibres of the nerve can be seen coming from a group of cells in the anterior portion of the anterior horn; at a higher plane the nucleus is situated further back and somewhat more internal; while at the

level of the olivary body it can be very distinctly located as a rounded mass immediately anterior to the central canal as it expands to form the ventricular cavity. As the twelfth nerve is purely efferent in function it has only one nucleus of origin. The ninth and tenth nerves, on the other hand, contain both afferent and efferent fibres, and therefore have double nuclei. The sensory or afferent fibres pass into a large nuclear mass of grey matter lying in the ventricular floor, immediately external to that of the hypoglossal, while the efferent fibres seem to be derived chiefly from cells in accessory nuclei, of which the most important is the nucleus ambiguus.

The origins and connections of the root fibres of the different cranial nerves shall, however, be discussed in greater detail later.

The **olivary body.**—The olive projects from the antero-lateral surface of the bulb between the pyramids and the restiform body, and can be easily recognised, both from its characteristic shape and from the nerves which pass out of the organ on both its anterior and its posterior aspects. It contains a central nucleus—the corpus dentatum—a flask-shaped fold of grey matter traversed by fine nerve-fibrils which belong more especially to the arcuate system, and which later enter the restiform body. This dentate nucleus (Fig. 411) is the most characteristic of the nuclei and contains a large number of nerve-cells imbedded in neuroglia. It is connected with the dentate body in the cerebellum. In addition to the olives we have two accessory olives, one situated below and internal to the dentate nucleus and the other superior and external. The root fibres of the hypoglossal emerge between the dentate nucleus and the internal accessory olive.

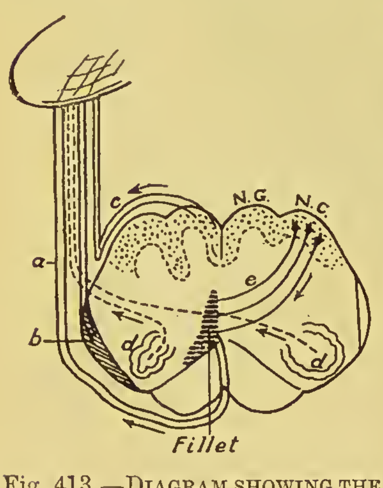

Fig. 413.—Diagram showing the Composition of the Restiform Body.

N.G., Nucleus gracilis; N.C., nucleus cuneatus; *a*, external arcuate fibres; *b*, direct cerebellar fibres; *c*, fibres from the nuclei gracilis and cuneatus; *d*, fibres from the olivary bodies; *e*, internal arcuate fibres.

The **restiform body.**—A term applied to the somewhat swollen postero-lateral portion of the medulla, from which the inferior peduncle of the cerebellum takes origin. It consists of both grey and white matter, the former derived from the contiguous cuneate nucleus and partly from the nucleus of Rolando, while the latter consists of fibres derived from many

sources, of which the more important probably are:—(1) The postero-lateral ascending tract of Flechsig; (2) the outer part of the homonymous cuneate nucleus; (3) the cuneate and gracilis nuclei of the other side, through the arciform system; (4) the dentate nuclei of both sides of the bulb (Fig. 413).

All these fibres apparently pass into the cerebellum from the cord and medulla, or are, in other words, centripetal; on the other hand, we have some which pass from the cerebellar cortex into the medulla, and possibly also the cord.

The restiform body is particularly evident in the upper levels of the medulla (Fig. 414), which we must now consider in detail. It will be seen that we are now above the level of the olivary body, though very frequently the upper portion of the nucleus can be made out. Other masses of grey matter can be observed, of which the more important are the superior olive and the nuclei of the auditory nerve. The superior olive is considerably smaller than the inferior, and, as we shall see later, is closely connected with the fibres of the cochlear division of the auditory nerve, the corpus trapezoideum, and the inferior corpora quadrigemina. In the anterior part of the section the arrangement of the elements follows closely the plan we have already seen in the lower levels of the bulb, but posteriorly certain very important modifications have taken place. The floor of the ventricle is now occupied by a very large mass of grey matter—the principal or dorsal nucleus of the eighth nerve—which is apparently connected with the vestibular root of that nerve, which circles round the anterior and mesial aspect of the restiform body to reach the nucleus. The postero-external aspect of the same body is surrounded by the dorsal or cochlear root, which, more especially in certain animals, exhibits a rounded swelling called the acoustic tubercle. In the triangle formed by the two roots and the ventral border of the restiform body lies

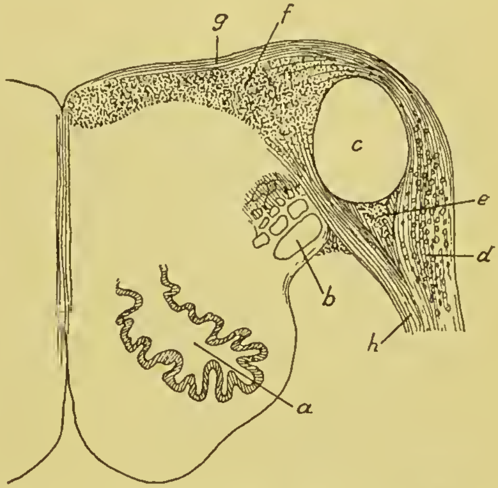

Fig. 414.—Transverse Section through Upper Portion of Medulla.

a, Upper part of olive; *b*, descending root of the fifth nerve; *c*, restiform body; *d*, cochlear root of the eighth nerve; *e*, accessory nucleus; *f*, principal or vestibular nucleus; *g*, striæ acusticæ; *h*, vestibular root of eighth nerve.

a collection of nerve-cells, forming the accessory nucleus of the auditory nerve.

The dorsal root requires, however, more than a mere passing mention, as it contains not only the fibres of the nerve but also a large number of somewhat elongated cells from which some of the fibres at least seem to take origin. The axons of the cells seem to divide, one branch passing towards the mid brain and cerebrum, the other entering the trunk of the nerve and running outwards to the cochlea.

Connections of the Spinal Cord with the Medulla.

The majority of the tracts in the spinal cord can be traced more or less distinctly into the medulla.

The fibres which ascend in the posterior columns of the cord (Goll and Burdach) pass into the upper swollen extremities of these tracts or clava and form synapses with cells lying in the central nuclei. The axons of these cells pass transversely across the bulb, as the internal arcuate fibres, to join the fillet which passes up through the pons and crus to the subthalamic region and the lateral portion of the optic thalamus. This tract is probably the chief path for the conveyance of afferent impressions to the cerebrum.

The postero-lateral ascending cerebellar tract (Flechsig) passes directly upwards into the corresponding portion of the bulb and assists in the formation of the restiform body; it is probable that the bulk of the fibres pass directly into the inferior cerebellar peduncle and thus enters the cerebellum, where they terminate in the grey matter of the vermis.

The antero-lateral ascending cerebellar tract (Gowers) enters the medulla between the olive and the restiform and then passes into the formatio reticularis; the fibres ascend in this network until they reach the crus, where they pass into the superior peduncle of the cerebellum and ultimately reach the cerebellar cortex. The origin of the fibres in the pyramidal tracts has been already mentioned and will be again discussed in connection with the course of the motor fibres.

The fibres in the pre-pyramidal tract (Monakow) do not form a distinct fasciculus in the medulla, but lie in scattered bundles in the formatio reticularis; in the pons, on the contrary, they lie in the region of the fillet, and therefore anteriorly to the network. They decussate in the crus—forming the anterior fountain decussation of Forel—and are probably derived from cells in the red nucleus.

Finally, it must be remembered that we have many bundles of fibres, longitudinal, transverse and oblique, which are confined to the crus, pons and medulla, and which terminate there in arborescences around cells in the formatio reticularis, the cranial nuclei, the olivary bodies, &c. Many of the fibres of the pyramidal tracts never reach the spinal cord, but synapse with cells in the grey matter of the medulla and pons; hence the volume of the pyramidal tract in the lower part of the bulb and in the spinal cord is considerably less than in the crus and pons.

The **pons varolii.** — As in the medulla, the arrangement of the nervous elements can only be ascertained by a study of sections through the organ at its various levels.

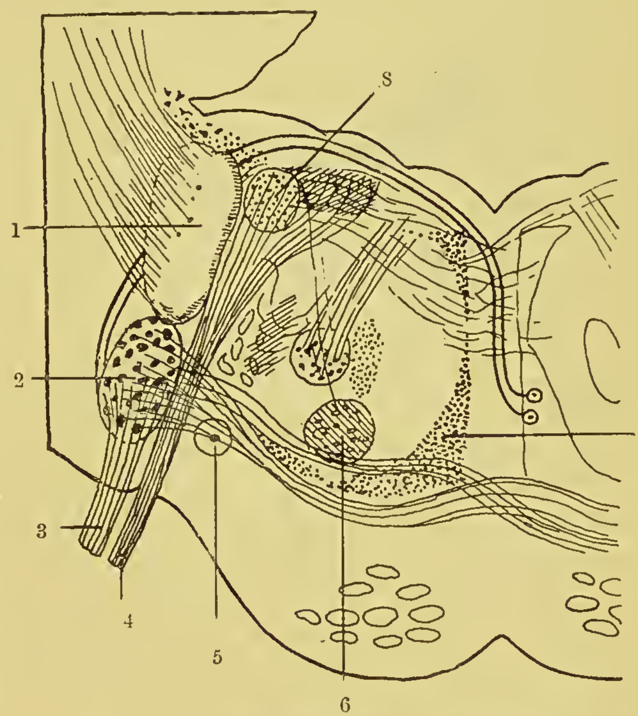

Fig. 415.—Transverse Section through Pons.

1, Restiform body; 2, accessory nucleus; 3, cochlear root; 4, vestibular root; 5, trapezium; 6, superior olive; 7, fillet; 8, Deiter's nucleus.

In the first section, taken through the organ immediately above the line of junction with the pons, and opposite the entrance of the auditory nerve, the most striking feature is the presence of large bundles of transverse fibres situated both anteriorly and posteriorly to the pyramidal tracts. The anterior or superficial transverse fibres are derived chiefly from the middle peduncle, and probably take origin in the grey matter of the cerebellar cortex; they cross the middle line and enter into synapses with the cells of the nuclei pontis. Many of the fibres seem to pass, however, in the opposite direction, namely, from the nuclei to the opposite cerebellar hemisphere. The deep transverse fibres belong to an entirely different system. They are especially numerous in some animals,

forming a very distinct body called the trapezium. They connect a number of small nuclei on each side of the pons in the immediate vicinity of the restiform body; of these the most important are the superior olive, the accessory nucleus of the eighth nerve, and the nucleus of the trapezium. The fibres also pass into the band of fibres known as the lateral fillet, and pass in that tract to the inferior quadrigeminal body and other nuclei in the mid brain.

From the relation of the fibres to the nuclei of the auditory nerve it is generally believed that they are concerned in the transmission of auditory impulses first to the other side of the pons and later to the cerebrum. The two roots of the eighth nerve are again seen surrounding the restiform body, and it will also be observed that the accessory nucleus has now become incorporated with the dorsal root, forming a single mass. Between the restiform body and the dorsal nucleus lie two structures, one somewhat anterior and the other posterior. The former is a band of longitudinal fibres (nature and distribution unknown), and the latter a group of large nerve-cells, forming a very distinct mass—the nucleus of Deiters, or, as it is sometimes called from its position, the lateral auditory nucleus. It extends from the middle third of the pons as far as the upper part of the medulla; in its upper third it lies above the dorsal auditory nucleus, while at the same time it passes backwards to lie in the floor of the ventricle. It can be seen in this posi-

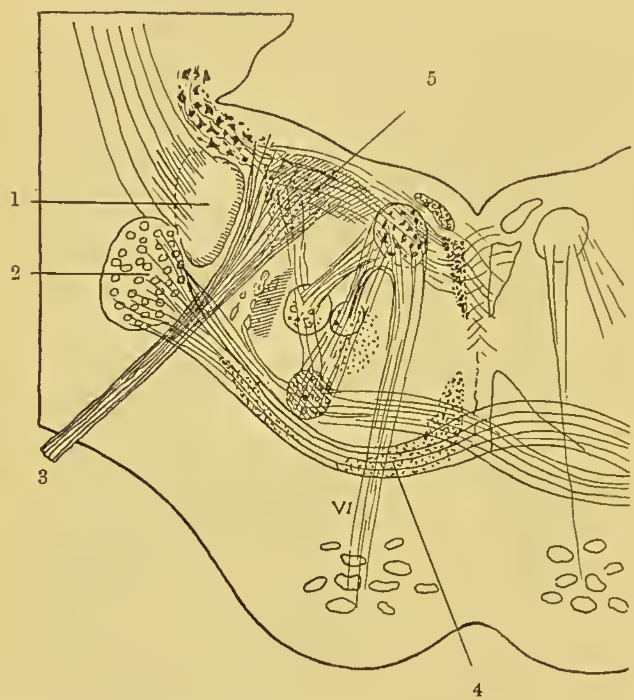

Fig. 416.—Transverse Section through Pons at the Level of the Vestibular Root.

1, Restiform body; 2, accessory nucleus; 3, vestibular division of eighth nerve; 4, trapezium; 5, dorsal nucleus.

tion in a section through the pons at the level of the nuclei of the sixth and seventh cranial nuclei (Figs. 415 and 416).

As the cells in Deiters' nucleus have synapses with several very important sets of fibres, we must consider it in some detail.

The nucleus seems to be very intimately connected with the cerebellum, for ablation of the homonymous hemisphere produces marked degeneration in its cells. It has also been shown by Monakow that section of the spinal cord produces a similar effect. Though the nucleus is often called the lateral auditory from its contiguity to the eighth nerve and its synapses with the fibres of the vestibular root, still the connection cannot be one of vital importance, as the cells do not degenerate after the nerve is divided. The cells are very large and give off several processes, the axons pass into the posterior longitudinal fasciculus and then divide, one branch passing upwards in that band as far as the subthalamic region and conveying impulses to the nuclei of the ocular nuclei, while the descending branch passes down through the medulla to enter the descending cerebellar tract of the cord (vestibulo-spinal fibres) and terminate in the ventral horn in synapses with the anterior multipolar cells.

A number of smaller nuclei are found in the vicinity of Deiters' nucleus: of these, the most important is one called the nucleus of Betcherew, which also seems to be connected with the vestibular root of the eighth nerve. Behind the trapezium lies a dense network of fibres, a continuation upwards of the formatio reticularis of the medulla. Many of the longitudinal fibres of this network belong to the system of the fillet in front and the posterior longitudinal fasciculus behind.

In Fig. 415, representing a section through the pons at the level of the nuclei of the sixth and seventh nerves, it will be seen that the general arrangement of the parts remains unchanged. The pyramidal bundles are, however, broken up into smaller fasciculi by the presence of the superficial transverse fibres. At the back of the formatio reticularis lie the nuclei of the cranial nerves given off at that level. In Fig. 416 the sixth nucleus is seen lying close to the middle line of the organ, while that of the seventh is somewhat anterior and lateral. The fibres of the seventh nerve sweep backwards towards the floor of the ventricle, and surround the nucleus of the sixth. Externally to the vestibular nucleus lies the upper end of Deiters' nucleus.

In the upper part of the pons several very interesting changes take place in the arrangement of the structural elements. In the first place the fourth ventricle is now narrowed down to form the

aqueduct of Sylvius, while two large bands of white matter pass from the sides of the organ to enter the lateral hemisphere of the cerebellum. These are the superior peduncles, and will be again discussed in the description of the crus cerebri. In the second place, if the section be taken above the origin of the cranial nerves (except the third and the fourth, which arise from groups of cells in the crus), no nuclei are seen, though a small group of cells is generally present, immediately in front of the aqueduct, which is most probably a prolongation downwards of the nucleus of the fourth nerve. At this level the fillet is a very distinct band lying in the front of the reticular formation, and generally divisible into two portions—a central and a lateral. As in the lower levels, the posterior longitudinal fasciculus lies at the back of the network.

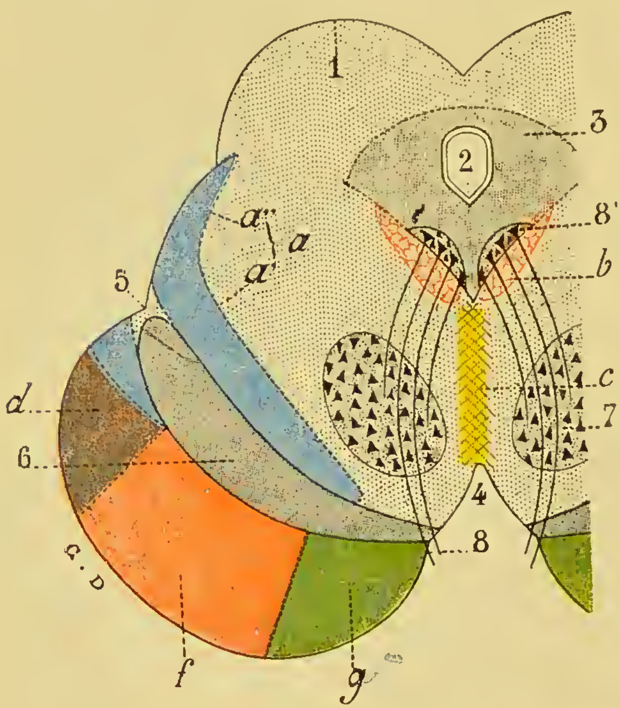

Fig. 417.—Scheme of the Structure of the Crus Cerebri (Testut).

1, Corpora quadrigemina ; 2, aqueduct of Sylvius ; 3, grey matter ; 4, anterior groove ; 5 and 6, substantia nigra ; 7, red nucleus ; 8 and 8′, third cranial nerve ; *a*, fillet ; *a*′, mesial ; *a*″, lateral ; *b*, posterior longitudinal fasciculus ; *c*, fountain decussations ; *d*, temporo-pontine projection system ; *f*, pyramidal projection system ; *g*, fronto-pontine projection system.

Crus cerebri.—The crus is incompletely divided into two portions by a mass of deeply pigmented matter — the substantia nigra — containing numerous nerve-cells of medium size which send processes into the contiguous white matter. The area in front of the substantia nigra is called the crusta, and that behind it the tegmentum.

The crusta contains in its middle portion the descending pyramidal fibres, again arranged in close formation, with masses of commissural fibres on each side belonging to the fronto-pontine and occipito-pontine projection systems (Fig. 418).

The posterior portion or tegmentum consists of a reticulum of very fine fibrillæ which in the upper part of the organ is of a peculiar character. The mesial or central part of the fillet lies immediately behind the substantia nigra, while the lateral part passes backwards towards the inferior quadrigeminal body.

Between the two crura, at the foot of the anterior groove, lies a mass of grey matter called the interpeduncular ganglion, which is connected by fine fibrillæ to the optic thalami on the one hand and the substantia nigra on the other.

Fig. 418.—Transverse Section through the Upper Part of the Crus.

1, Aqueduct of Sylvius; 2, third motor nucleus; 3, posterior longitudinal fascia; 4, red nucleus; 5, fountain decussations; 6, third nerve; 7, frontal projection system; 8, pyramidal projection system; 9, caudate projection system; 10, temporal projection system; 11, substantia nigra; 12, median fillet; 13, lateral fillet; 14, brachium; 15, anterior quadrigeminal body.

The transverse fibres of the tegmentum seem to be derived from quite a number of sources; of these, two are apparently of special importance, namely the superior peduncle of the cerebellum, and at a higher level the corpora quadrigemina and corpora albicantia. The superior peduncle consists of white fibres which enter the crus on its postero-lateral aspect and then pass across the mesial line behind the tract of the fillet, forming a well marked decussation. Many believe that the fibres then bifurcate, one branch passing upwards to end in synapses with the cells of the red nucleus while the other passes down into the pons and medulla and assists in the formation of the descending cerebellar tract. At a higher level the transverse fibres are chiefly derived from the quadrigeminal bodies and the corpora albicantia. The former

sweep round immediately anterior to the nuclei of the third and fourth cranial nerves and posterior longitudinal fasciculus and cross the mesial line, forming the posterior or fountain decussation of Meynert; they then pass down the tegmentum, forming a small bundle called the ventral longitudinal fasciculus, which later unites with the posterior bundle, forming a single tract, which enters the antero-lateral region of the spinal cord and enters into synapses with the ventral cells. In addition to this posterior fountain decussation of Meynert we have also an anterior one, called the fountain decussation of Forel, which seems to be formed chiefly by fibres derived from the cells of the red nucleus and the corpora albicantia; these fibres pass down to enter the pre-pyramidal tract of the cord, and synapse chiefly with the cells of the crescent.

Several other tracts have been described in the crus, but they are of small size, and are so imperfectly traced out that little or nothing of a definite character is known regarding them.

In the upper part of the tegmentum lies a large rounded mass of cells called the red nucleus. The cells have extensive synapses with the fibres of the posterior longitudinal fasciculus, the fillet, and the ascending branches of the fibres contained in the superior peduncle. The axons of the cells pass down through Forel's decussation, as we have just seen, to enter the medulla and cord. The nucleus is traversed by the fibres of the third cranial nerve, though they do not seem to have any direct connection with its cells.

The Optic Thalamus and the Subthalamic Region.

We must now pass to consider the connection between the crus cerebri and the great brain, and in doing so it will be necessary first to study the optic thalamus and the region immediately beneath. The optic thalamus is a large ovoid mass of grey and white matter situated on a forward projection of the tegmentum of the crus, called the subthalamic region; it lies in the antero-posterior plane, and consequently lies somewhat across the crus, so that the crusta and its upward prolongation—the internal capsule—lie ventro-laterally to the nucleus.

The subthalamic region, like the tegmentum, consists of a network of fibres containing numerous nerve-cells. Three layers can be distinguished—a "stratum dorsale," situated immediately below the thalamus; a "zona incerta," or intermediate layer consisting of a nervous reticulum continuous with that of the tegmentum; and

an inferior or "nucleus of Luys," frequently called the corpus subthalamicum, apparently related closely to the substantia nigra. From these layers fibres are given off which sweep into and around the posterior limb of the internal capsule to the lenticular nucleus and the lateral cerebral cortex. One band of these fibres is peculiarly distinct, and is called the ansa lenticularis.

In the stratum dorsale, which we might consider to be the continuation of the posterior part of the tegmentum, we find numerous fibres derived from the posterior longitudinal fasciculus and also from the upper end of the red nucleus.

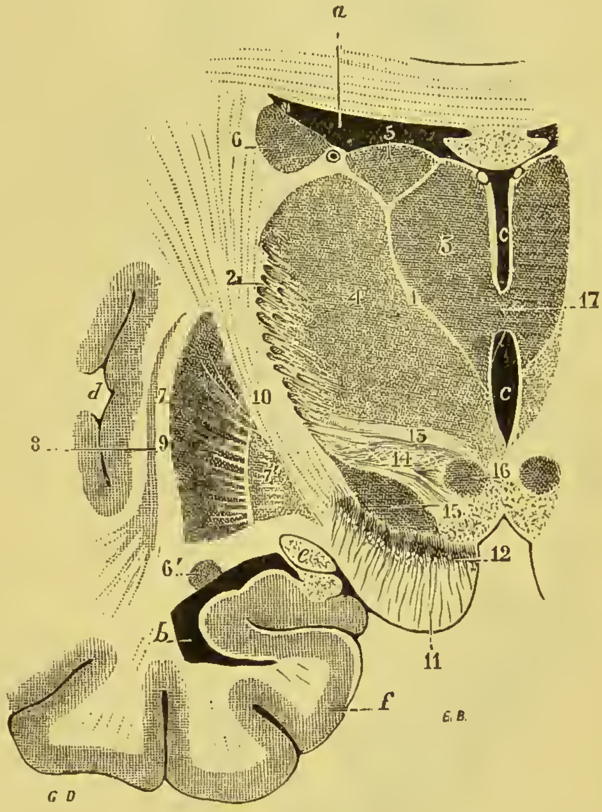

Fig. 419.—Section through the Basal Ganglion.

1, 2, 3, 4, 5, The optic thalamus, showing the various ganglia; 6 and 6′, caudate nucleus; 7 and 7′, lenticular nucleus and putamen and nucleus pallidus; 8, claustrum; 9, external capsule; 10, internal capsule; 11, crusta of the crus; 12, substantia nigra; 13, stratum dorsale; 14, zona incerta; 15, nucleus of Luys.

The optic thalamus itself contains a considerable quantity of grey matter imperfectly divided into several nuclei. Of these, one lies in the anterior portion of the ganglion and contains a number of very large nerve-cells, which are indirectly connected by the fibres of Vicq d'Azyr to the corpora albicantia and the anterior pillars of the fornix. The mesial nucleus, situated in the inner portion of the ganglion, and immediately external to the cavity of the third ventricle, is connected to its fellow of the opposite side by the middle or grey commissure. The third or postero-lateral nucleus forms the inner boundary of the posterior limb of the internal capsule and projects backwards, forming a

rounded mass called the pulvinar ; the outer edge of this nucleus has a curious irregular or lacerated appearance from the passage of vast numbers of nerve-fibres into the adjacent posterior limb of the internal capsule on their way to the lenticular and caudate nuclei of the corpus striatum and the cerebral cortex.

One group of fibres which passes backwards from the hinder part of the thalamus to the occipital lobes is particularly distinct, and is designated the optic radiation of Gratiolet.

The thalamus is also connected to the other nuclei in its immediate vicinity, namely the corpora quadrigemina and the corpora geniculata.

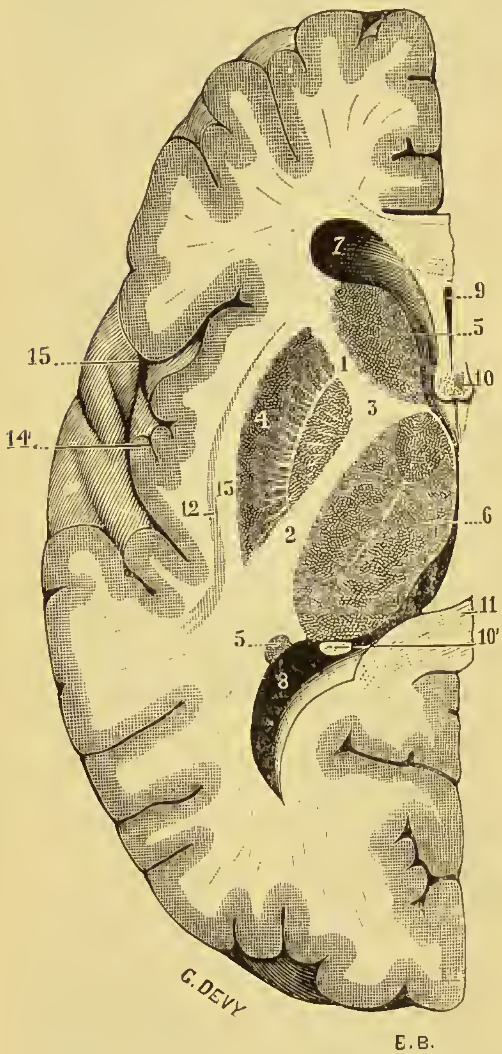

Fig. 420.—Transverse Section through the Basal Ganglion.

Internal Capsule.—1, Anterior limb; 2, posterior limb ; 3, genu ; 4, lenticular nucleus ; 5, caudate nucleus ; 6, optic thalamus ; 7, anterior horn of the lateral ventricle ; 8, posterior horn ; 9, fifth ventricle ; 10, fornix ; 11, corpus callosum ; 12, claustrum ; 13, external capsule ; 14, island of Reil.

The Internal Capsule.

As this area is one of extreme importance from both a physiological and a clinical standpoint, we must consider it in some detail. It is a belt of white matter lying between the optic thalamus and the caudate nucleus on the inner side and the lenticular nucleus on the outer. The character of the area depends considerably on the plane in which the section is taken ; in a horizontal section through the middle of the optic thalamus it presents the appearance shown in Fig. 420. It consists of three parts—an anterior limb, a genu or knee, and

a posterior limb; the junction of the two limbs forms an angle of about 120 degrees.

Composition of the internal capsule.—As the posterior limb is the upward prolongation of the anterior part of the crus, or crusta, we should naturally expect to find that it contains the same fibres, and in great part this is the case. The longitudinal fibres which pass down in the capsule belong to four projection systems, one coming from the Rolandic areas, and called the pyramidal or pedal system, a second from the anterior parts of the cerebral cortex, and therefore termed the frontal projection, while the third lies posteriorly and is composed of fibres derived from the cortical grey matter in the occipital and temporal regions. The fourth does not originate in the cortex, but in the grey matter of one of the basal ganglia, namely the caudate nucleus of the corpus striatum.

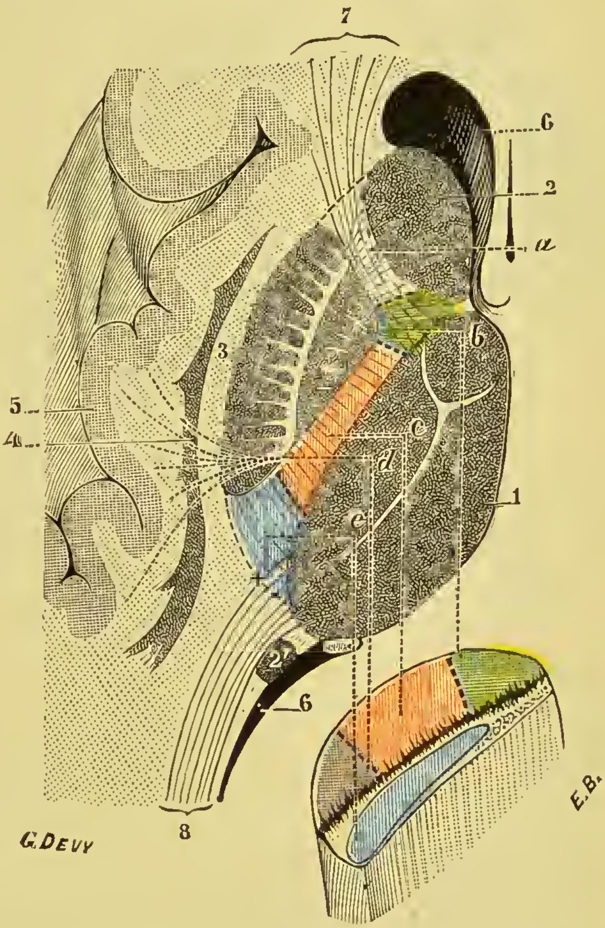

Fig. 421.—Scheme of the Connections of the Crus with the Basal Ganglia (Testut).

1, Optic thalamus; 2, caudate nucleus; 3, lenticular nucleus; 4, claustrum; 5, grey matter of the island of Reil; *b*, fronto-pontine projection system; *c*, pyramidal projection system; *d*, temporo-pontine projection system; *e*, sensory fibres; 7, frontal fibres; 8, optic radiations.

The fibres in the first or pedal system form a mass lying in the middle portion of the capsule, namely, in the genu and the anterior part of the posterior limb. The various fasciculi which go to supply the

various parts of the body are arranged in fairly definite formation; thus in the genu we have the fibres which supply the muscles of the eye, head, tongue and mouth, while in the posterior limb we find, from before backward, those supplying the arm, abdomen and lower limb.

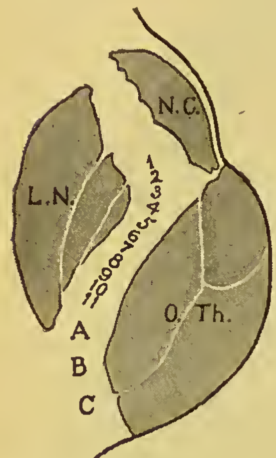

Fig. 422.—Scheme Illustrating the Relative Position of the Different Bands of Fibres in the Internal Capsule.

N.C., Nucleus caudatus; O.Th., optic thalamus; L.N., lenticular nucleus. The anterior limb of the capsule contains, in front the fibres of the fronto-pontine projection system, and posteriorly some of the fibres of the pyramidal system — 1, fibres to head; 2, head; 3, tongue. The posterior limb contains—4, mouth; 5, arm; 6, hand; 7, trunk; 8, hip; 9, knee; 10, leg; 11, toes. In the posterior part we have sensory fibres A, the temporo-pontine projection fibres B, and the visual radiating fibres C.

We have already traced the fibres of this system down through the crus, pons and medulla into the cord, so that we shall now pass on to consider the other projection systems we have mentioned. The frontal system occupies the anterior limb of the capsule and then passes down into the crusta, where it lies on the mesial aspect of the pyramidal fibres (Fig. 418). In the pons the fibres terminate in arborescences apparently around the cells of the nuclei pontis and the transverse fibres, so that the tract has consequently a connection with the contra-lateral cerebellar hemisphere.

The posterior projection system is also very well marked. It occupies the posterior part of the internal capsule, immediately behind the pyramidal tract, and later enters the crus, where it lies in the outer portion of the crusta. Like the fibres of the frontal system they also have extensive synapses with the cells of the nuclei pontis. These three projection systems are chiefly composed of "descending" fibres, for lesions in the various regions of the cortex in which the fibres take origin are followed by degeneration downwards through the corona radiata to the internal capsule and parts beneath; a certain number of ascending fibres are, however, also present, more especially in the posterior or occipito-temporal system.

The fourth projection tract is very much smaller in size; the fibres have apparently no connection with the cerebral cortex, as they do not degenerate after ablation of the grey matter. They are more or less incorporated with the fibres of the frontal system in the anterior limb of the capsule, but form a distinct band in the crus, immediately behind the pyramidal

tract. The fibres seem to end in synapses in the substantia nigra and in the pons.

Blood supply of the internal capsule.—This is a matter of very great importance, as rupture of the vessels and hæmorrhage is of frequent occurrence. The basal ganglia are supplied by three sets of arteries derived from the middle cerebral, called the lenticular, the lenticulo-optic and the lenticulo - striate respectively. These break up into a series of terminal twigs which do not anastomose with one another in the usual way. Of the lenticulo-striate system, one artery is especially large; it passes to supply the outer part of the putamen, and from its tendency to rupture it has been named by Charcot the artery of cerebral hæmorrhage.

Fig. 423.—Scheme of the Blood Supply of the Internal Capsule (Testut).

5, The lenticulo-striate system of vessels; 5′, the artery of cerebral hæmorrhage; *c*, caudate nucleus; *b*, lenticular nucleus; *d*, optic thalamus.

The **corpus striatum.**—A large ganglion lying anteriorly and externally to the optic thalamus, and containing two large nuclei called the caudate and lenticular respectively.

The *caudate nucleus* is much the larger of the two, and consists of a large rounded anterior portion or head, which lies in the floor of the lateral ventricle and forms also the posterior boundary of its anterior horn. The ventricular portion of the nucleus is marked off posteriorly from the optic thalamus by a white band called the tænia semicircularis, but this does not represent its posterior limit, as it passes backwards superiorly to the lenticular nucleus as far as the lateral horn, when it descends as a fine tail-like process in the roof of that cavity. It is of a

somewhat dark colour, resembling that of the putamen of the lenticular nucleus, and contains numbers of cells from which the fibres of the caudate projection system take origin. Both anteriorly and inferiorly the grey matter is directly continuous with that of the lenticular nucleus, and numerous fibres pass between the two, which are probably derived primarily from the tegmental and thalamic regions.

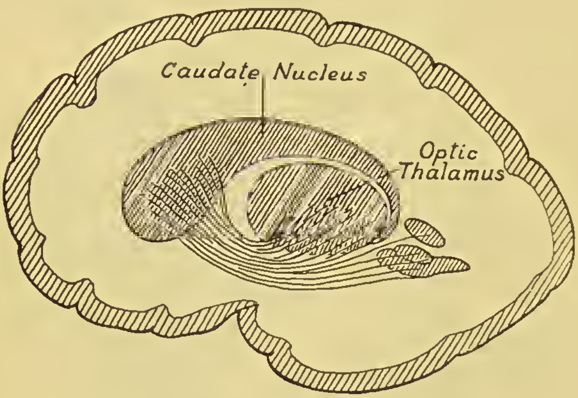

Fig. 424.—Diagram of the Relations of the Basal Ganglia.

The *lenticular nucleus* consists of an inner portion, which is light in colour and consequently called the globus or nucleus pallidus, and an outer, darker part or putamen. The inner border of the nucleus pallidus, like the opposing edge of the optic thalamus, has a reticular or irregular character from the entrance of nerve-fibres from the adjacent posterior limb of the internal capsule. The pale portion of the nucleus is again subdivided into two parts by the presence of a large band of white fibres, some of which pass later into the grey matter of both the nucleus pallidus and the putamen, while others run upwards either to terminate in the caudate nucleus or to join the corona radiata and thus reach the cerebral cortex. One band of fibres is especially distinct, and is called the ansa lenticularis.

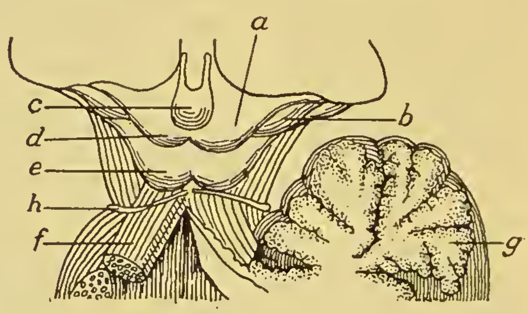

Fig. 425.—Relations of the Corpora Quadrigemina.

a and *d*, Superior quadrigeminal body; *b*, geniculate body; *c*, pineal gland; *e*, inferior quadrigeminal body; *f*, superior peduncles of the cerebellum; *g*, cerebellum; *h*, fourth nerve.

The **corpora quadrigemina**.—A group of four small bodies situated posteriorly to the optic thalami, and above and behind

the crus cerebri. Each body is prolonged laterally into a process or brachium which passes forwards and outwards under cover of the swollen posterior end of the thalamus or pulvinar to enter the optic tracts or the geniculate bodies.

The *inferior* pair, or testes, are intimately connected with two areas, namely, the tegmental region of the crus and the internal geniculate body. In Fig. 418 it will be seen that the fillet is divided into a mesial and a lateral portion; the latter passes towards the inferior quadrigeminal body and terminates in the central mass of grey matter in that ganglion. The fibres of the lateral fillet seem to be principally derived from the trapezial system in the pons, and from the cells in the acoustic tubercle on the cochlear root of the eighth nerve. Of the two, the former is probably the more important; some of the fibres are those of the deep transverse system, while others are the axons of cells in the superior olive, the nucleus of the trapezium and the accessory nucleus of the auditory nerve. From the origin of the fibres, it is very possible that the tract is a portion of the auditory pathway, and that the inferior quadrigeminal body is concerned with the reception or transmission of auditory impulses, and we have both comparative and experimental evidence in support of this contention.

The *superior* corpora quadrigemina.—In certain of the lower animals, such as the birds and reptiles, where vision is peculiarly acute, the anterior pair are extremely developed, forming the optic lobes. The chief connections of the ganglia are with the optic tracts and the crura cerebri. The lateral brachium passes directly into the optic tract and has connections with the external geniculate body and, in many animals, the pulvinar of the optic thalamus. The close connection between the bodies and the optic mechanism can be demonstrated by excising the eye in a newly-born animal, or by simply dividing the optic nerve, when atrophic changes set in in the ganglion cells.

While undoubtedly very large numbers of afferent fibres pass from the optic tracts into the nucleus, comparatively few pass from it to the occipital lobes, where, as we shall see later, the analytic visual centres are situated. It is probable, therefore, that the incident impulses which pass to the nates through the optic tracts travel later not to the centres concerned in the psychological portion of the visual mechanism, but rather to those involved in the reflex movements of the eyeballs, the pupil and the ciliary muscle.

Again, electrical or indeed any form of stimulation of the nates produces results closely associated with the visual reflex mechanism,

such as movements of the eyeballs, variation in the size of the palpebral fissure, of the diameter of the pupil, &c. These effects are chiefly dependent on the connection of the nates with the nucleus of the third nerve in the crus. In the first place, a large number of ascending fibres pass to the ganglia through the mesial band of the fillet, and to a lesser extent through the lateral fasciculus. By this connection the nates become included more or less directly in the chief spino-cerebral pathway. Secondly, a band of fibres emerges from the central mass of grey matter in the nuclei, and passes forwards into the tegmental region immediately in front of the grey matter of the aqueduct and decussate, forming the posterior decussation of Meynert we have already described in that area. Some of the fibres apparently pass to the nuclei of the third nerve, while the rest enter the longitudinal bundle and synapse with the other ocular nuclei, namely, the fourth and the sixth, as well as with other groups of nerve-cells, both in the medulla and the spinal cord. Another outgoing fasciculus of fibres seems to pass more especially to the red nucleus, and, according to Held, appears to be of considerable importance.

Corpora geniculata.—Two small nuclei lying in close relation to the pulvinar of the optic thalamus and the optic tracts. From their position they are called external or lateral, and internal or mesial. The external are very closely connected to the optic tracts and the lateral brachia of the anterior quadrigeminal bodies, and are apparently of very great importance in vision, as a cell station on the ingoing pathway. Large numbers of fibres enter the nucleus and terminate in synapses with cells, which, in turn, send on axons to the occipital cortex. In the majority of animals this nucleus, indeed, seems to be the most important link in the psycho-visual path, just as the anterior quadrigeminal body is in the reflex visual one.

The internal geniculate body, though it is anatomically connected very closely with the optic tracts, does not seem to be closely related to it from a functional point of view, as it does not degenerate after section of the optic nerve or excision of the eyeball. Its most important connection is with the inferior quadrigeminal body, and, like this nucleus, it is probably related closely to the auditory mechanism.

The **corpora albicantia, or corpora mammillaria.**—Two round nuclei situated on the base of the brain immediately behind the optic chiasma, and closely connected with the anterior pillars of the fornix, which enter the nuclei from above and wind round

their central masses of grey matter. The bodies are also connected with the anterior part of the optic thalamus and with several nuclei in the crus. The thalamic connection is established through the bundle of Vicq d' Azyr, a mass of white fibres which passes up to the ventral nucleus of the thalamus, though the exact termination of the fibres is somewhat doubtful, while the other is formed by the bundle of v. Gudden, which passes into the ventral part of the tegmentum and assists in the formation of the anterior fountain decussation of Forel. Some of the fibres terminate in synapses in the interpeduncular ganglion.

Between the internal capsule and the basal ganglia on the one hand, and the cerebral cortex on the other, lies a great mass of white matter called the corona radiata, consisting of the centrifugal fibres belonging to the great projection systems and the centripetal fibres passing from the optic thalamus, &c., towards the cortex cerebri.

The **cerebral cortex.**—The cortex, like the grey matter of the cord and the mid-brain, consists of a mixture of nerve-fibres, medullated and non-medullated, and nerve-cells, which vary considerably in their characters. The nerve-fibres run both longitudinally and transversely, and are more distinct in the deeper parts of the grey matter, while the cells are more or less perfectly disposed in certain layers. As there is no sharp line of demarcation between the layers, a various number have been described by different histologists. Perhaps the simplest and most satisfactory general classification is into four layers. Of these, the first or superficial contains a very few cells but a well-marked entanglement of nerve-fibrillæ, and is consequently called the molecular layer. The cells which are present are small in size and somewhat flattened, with axonic processes which pass away horizontally from the bodies of the cells, parallel to the surface; these processes synapse partly with a large number of fibrillæ derived from the dendrites of the pyramidal and other cells found in the deeper layers, and partly with the terminal arborescences of fibres coming from the basal ganglia and the tegmental region, and probably carrying afferent impulses from the cord, &c., to the cortex. A few neuroglia cells are also present. In a preparation stained by Golgi's method this surface layer appears very dark from the density of the reticulum exhibited by the deposition of the silver. Below this superficial layer lies a second, containing a large number of nerve-cells, of which the bulk are pyramidal in shape. While these cells are all more or less alike in shape, they vary greatly in size from small ones of about 10 μ to very

large types or giant pyramidal cells, which may be 120 μ or even more. As a general rule, the smaller cells are found nearer the surface, and in some cases form a distinct layer—the layer of small pyramidal cells—of considerable thickness. The medium or large-sized pyramidal cells form, then, the third layer, and in certain portions of the cortex, such as the motor areas, they are arranged in clusters—the cell nests of Betz. As these cells are apparently of great importance, we must consider them in some detail.

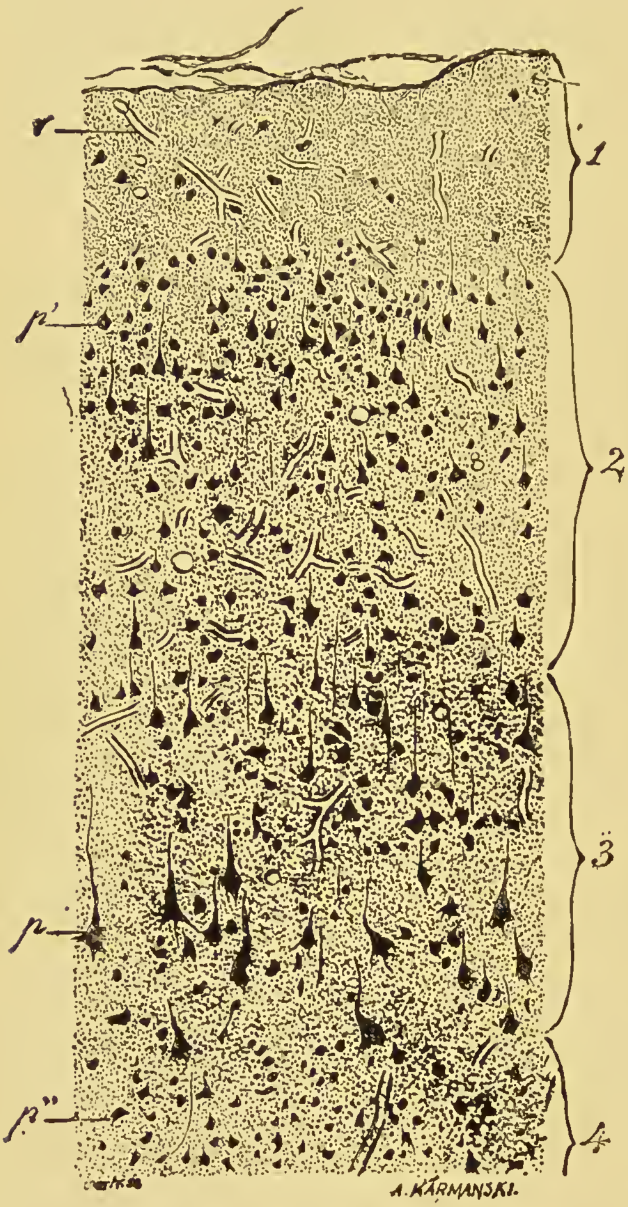

Fig. 426.—Vertical Section through the Cerebrum.

From the base, sides and apex of the cell, processes are given off which pass into the surrounding tissue. The axon, which is slender, passes down from the base of the cell to enter the subjacent white matter, while the dendrites break up chiefly in the immediate vicinity of the parent cell. The apical dendrite is generally the best developed and runs up into the superficial layer, where it assists in the formation of the nervous

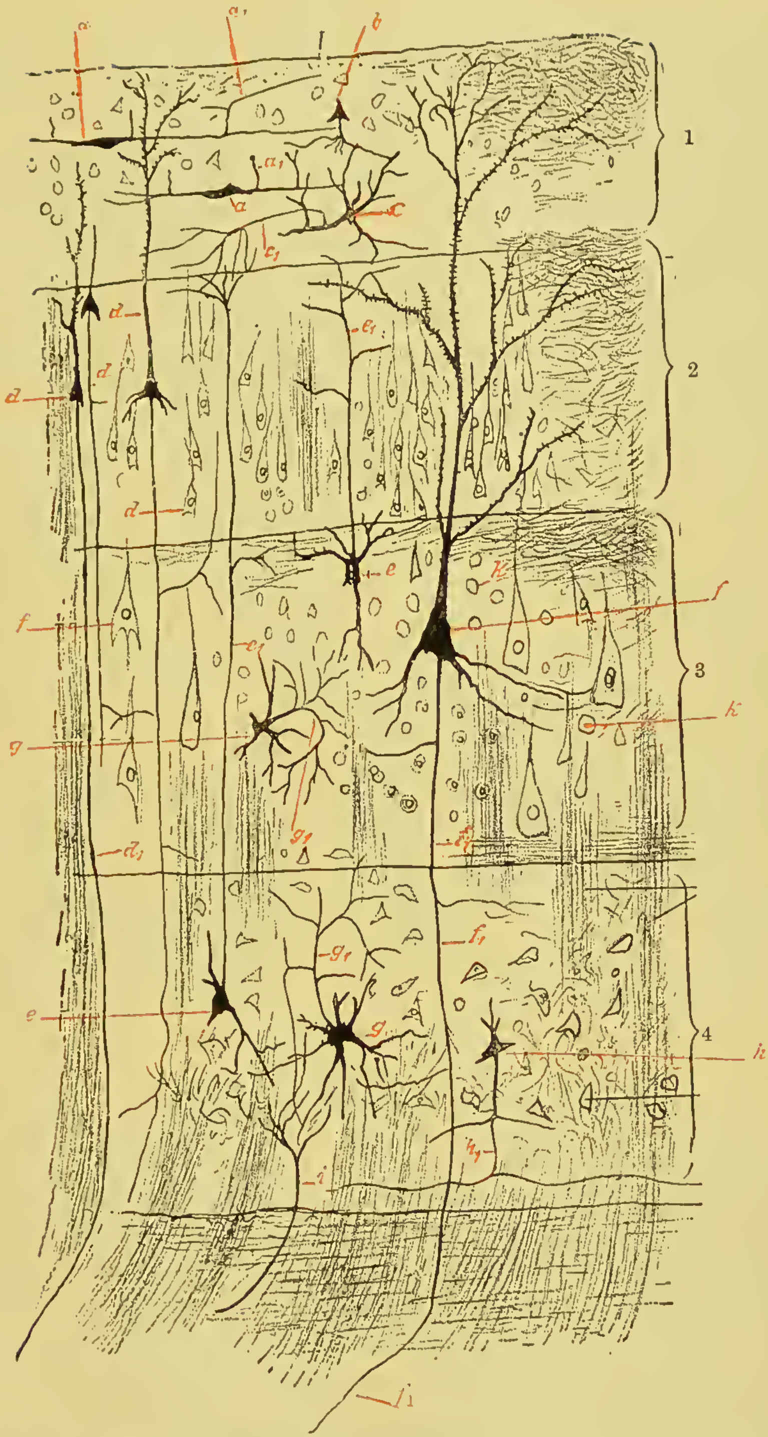

Fig. 427.—Vertical Section through the Cerebrum (Monakow).

(1) *a*, Fusiform cells; *b*, small triangular cells; *c*, small polygonal cells. (2) *d*, small pyramidal cells; *e*, cells of Martinotti. (3) *f*, Grant pyramidal cells; *g*, Golgi cells. (4) *h*, polymorphic cells.

entanglement we have already spoken of. In Golgi specimens the dendrites have a peculiar and highly characteristic spiculate character.

Below the zones containing the larger and smaller pyramidal cells lies a fourth or polymorphic cell layer, in which the cells are small and irregular in shape. The most characteristic cell in this layer is the polymorphous or granule cell. On section it has frequently a stellate appearance. The dendrites generally ramify in the pyramidal layers and rarely extend as far as the surface. The axons, as in the case of the pyramidal cells, pass down into the corona radiata. These cells are found in immense numbers in the areas which seem to be essentially sensory in function, such as the occipital lobe, where the pyramidal cells are correspondingly reduced both in number and in size. In these areas they are not confined to the lower layers, but are usually scattered throughout the breadth of the grey matter below the superficial layer. In some cases the axons of the polymorphic cells seem to pass upwards to the surface and to take part in the general ramification found in the superficial layer.

Subjacent to the polymorphic layer, and incorporated with it, we find a zone containing a number of cells, generally of a fusiform character; not infrequently the band is of considerable breadth, and then forms a fifth or fusiform cell layer of the cortex.

In both the pyramidal and the polymorphic layers numerous smaller cells can be seen, some with processes which pass upwards into the superficial layer (cells of Martinotti), and others belonging to Golgi's second type of cells, in which the axon breaks up immediately into a terminal arborescence in the immediate vicinity of the body of the cell. Neuroglia cells are also found in these layers.

The nerve-fibres can be divided into two sets—perpendicular and transverse. The former pass into the grey matter from the corona radiata in bundles which later open out and are consequently less distinct in the outer zones. They consist not only of the axons of the pyramidal and polymorphic cells of the cortex, but also of the various afferent fibres which are derived from the basal ganglia, &c., and which ultimately ramify in the superficial layer. The transverse fibres are somewhat imperfectly arranged into fasciculi; of these, one is generally distinguished in the small pyramidal cell layer and a second in the region of the larger pyramids, these being called the outer and inner bands of Baillarger. In the superficial layer many of the fibres are arranged parallel to the surface (tangential fibres), forming a third transverse band.

Many of these transverse fibres are probably derived as collaterals from the axons of the pyramidal cells, while others are the axons of cortical cells which are probably commissural in function. It will therefore be apparent that the grey matter of the cerebral cortex, like that of the spinal cord, is essentially an entanglement of fibres and cells in which the various constituents are brought into close relationship with one another, so that nerve impulses can readily be transmitted from one neuron to another and thus complex and co-ordinate results be obtained. In other words, each cell in the cerebral cortex cannot be considered an independent functional unit, though it may be anatomically distinct, and we must now describe in some little detail the chief

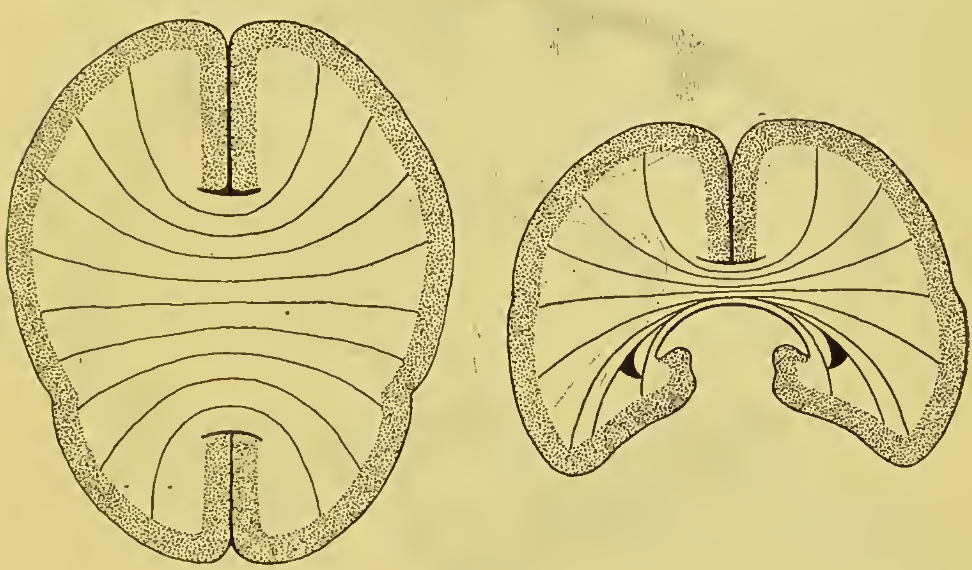

Fig. 428.—Corpus Callosum.

bands of commissural fibres which link together the different parts of the brain and assist in the production of this co-ordinate action. The commissural tracts can be roughly divided into two groups, one consisting mainly of transverse fibres, such as the corpus callosum, and a second containing longitudinal or oblique fibres which pass chiefly between gyri on the same side of the cortex (Fig. 429), such as the cingulum, &c.

The **corpus callosum**.—This is composed almost entirely of white fibres which pass between the two cerebral hemispheres; they plainly connect homologous areas, such as the two parietal

lobes, though this is by no means always the case. Anteriorly and posteriorly the fibres sweep away from the general mass to enter the frontal and the occipital lobes respectively, forming in the one instance the forceps major, and in the other the forceps minor. A certain number of the fibres, however, do not seem to pass to the contra-lateral cortex, but, instead, enter the pyramidal projection system; for ablation of the "motor" areas of the one hemisphere sets up degenerative changes which can be traced down the opposite pyramidal tracts both in the internal capsule and the crus. Some of the callosal fibres appear to be the axons of cells in the cortex, though many are doubtless col-

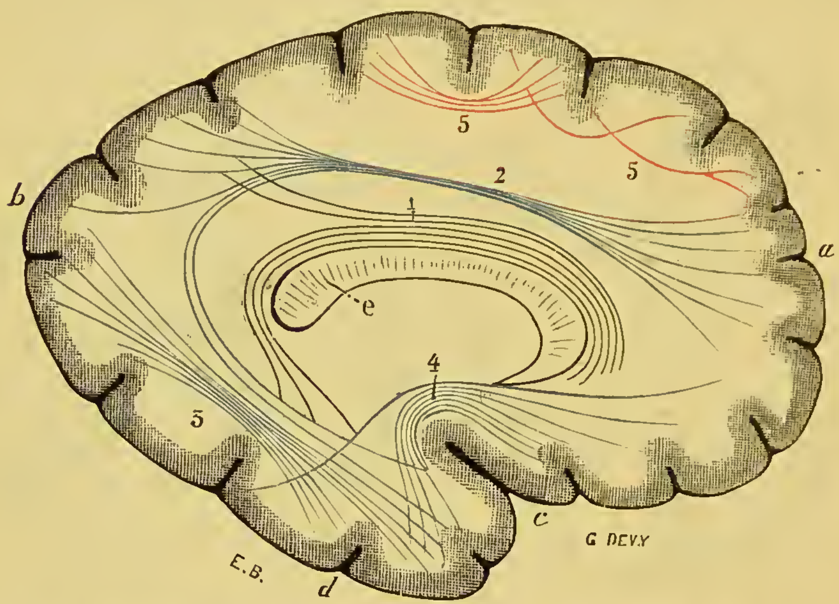

Fig. 429.—Position of the Chief Bands of Association Fibres (Testut).

a, Anterior, and *b*, posterior end of the hemisphere; *c*, fissure of Sylvius; *d*, temporal lobe; *e*, splenium of the corpus callosum; 1, cingulum or fronto-temporal fasciculus (in limbic lobe); 2, the superior longitudinal fasciculus (fasciculus arcuatus), linking the frontal with the occipital gyri; 3, the inferior longitudinal (occipito-temporal) fasciculus; 4, the unciform (fronto-temporal) fasciculus; 5, fibres passing between adjacent gyri.

laterals derived from the axons of the fibres of the various projection systems we have already described. The corpus callosum also contains a number of longitudinal fibres arranged in bands and called the striæ longitudinales, well seen on the upper aspect of the commissure. Anteriorly these fibres form peduncles which pass into the temporal lobes and appear to have extensive connections there, while posteriorly they pass chiefly to the hippocampal convolution.

The **anterior commissure.**—This is an extremely important commissure in lower animals, in which the corpus callosum is either absent or imperfectly developed. It consists of fibres derived from cells situated chiefly in the temporal lobes, which pass in convergent fashion through the lenticular nucleus to form a well-marked transverse band somewhat anteriorly to the anterior pillars of the fornix.

The **posterior commissure.**—Posteriorly to the third ventricle and under cover of the anterior corpora quadrigemina lies a third or posterior commissure containing fibres which seem to pass from the tegmental region and the optic thalamus to the contra-lateral cerebral hemisphere.

In addition to these large transverse commissures we have a large number of smaller ones, which pass either between adjacent convolutions (short association bands) or between the different lobes, such as the temporal and the occipital, the temporal and the frontal, &c. (long association bands) (Fig. 429).

The Cerebellum.

The cerebellum consists of two lateral portions or hemispheres united by a central lobe called the vermis or worm. Like the cerebrum, it consists of an outer zone of grey matter enclosing an inner mass of white. The cortex is excessively convoluted and shows on section a peculiar arborescent appearance from which it is commonly called the arbor vitæ! When stained by ordinary methods, as with hæmotoxylin and eosin, each convolution or leaflet shows three distinct zones—an outer, which stains lightly and contains comparatively few cells—the molecular layer; an intermediate, darkly stained and containing a very large number of small cells—the granular or rust-coloured layer; and in the centre a zone composed of

Fig. 430.—Vertical Section of Cerebellum (Human).

a, Core of white matter; *b*, nuclear layer of grey matter; *c*, molecular layer of grey matter; *d*, Purkinje cells; *f*, pia mater.

Fig. 431.—Vertical Section of Cerebellum (Human).

a, Pia mater; *b*, molecular layer of grey matter; *c*, granular or nuclear layer of grey matter; *d*, white core; *e*, Purkinje's ganglion cells (antler cells).

ordinary nerve-fibres. Between the molecular and the granular layers lies a very distinct row of large and prominently nucleated cells called the antler or ganglion cells of Purkinje.

In sections stained by Golgi's method, the various cells and processes found in the different layers can be distinctly traced. In the molecular zone we find only a few cells, some nervous and others neurogliar. Of the former, the most important are some small stellate cells giving off slender axons which pass along parallel to the surface of the leaflet and send off collaterals that pass perpendicularly downwards to end in synapses around the upper part of the bodies of the Purkinje cells. They are called basket-cells from the character of their terminal arborescences. The most conspicuous elements in the layer, however, are the arborescences of the dendrites of the Purkinje cells, especially if the specimen be cut in certain planes; these can be readily recognised both by their attachment to the cell below and the character of their arborescence in the layer. The cell is ovoid in shape and prominently nucleated. From the upper part a thick dendrite is given off which divides almost immediately into its terminal arborescence, somewhat resembling

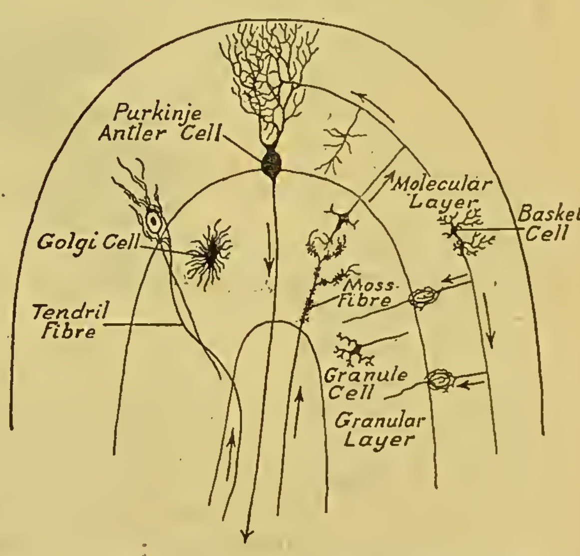

Fig. 432.—Scheme of the Position and Relation of the Cerebellar Cells.

the branchings of the antlers of a stag. The axon is given off from the lower part of the cell and passes directly into the granular layer, and later into the white centre of the leaflet, where it gives off collateral twigs.

Several types of cells are found in the granular layer; of these a small granule cell is the most frequent. This cell possesses three or four dendrites which ramify in the immediate vicinity of the cell body and an axon which passes upwards into the molecular layer and there divides into two branches, which run along horizontally in that layer and interweave with the dendrites of the Purkinje cells. Several cells belonging to the second type of Golgi are also found in this layer and ramify widely in its substance.

The white matter consists of medullated fibres passing to and from the cerebellar cortex. Those coming from the grey matter, or, as we may call them, the descending fibres, are chiefly the axons of the Purkinje cells. Of the ascending fibres we seem to have two chief types—one passing up into the molecular layer and there forming a climbing network around the dendrites of the Purkinje cells, and consequently called a tendril fibre. The second type of fibre ends in the granular layer in synapses with the granule cells, though a few may pass upwards into the molecular zone. It is characterised by the presence of curious little tuft-like excrescences, and has consequently been called by Cajal a moss fibre. It will be apparent from the relation of these structures to one another that the Purkinje cells are closely related to several groups of fibres; in the first place, the body of the cell is invested by the basket-like reticulum derived from the descending processes of the cells in the molecular layer, while, secondly, the dendrites are embraced by the tendril fibres coming

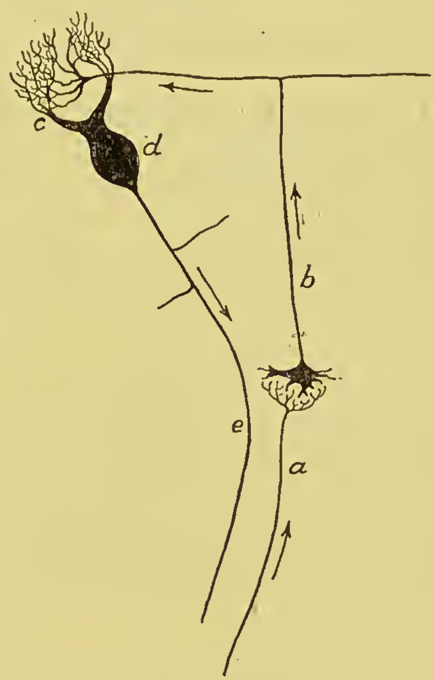

Fig. 433.—Relation of the Purkinje Antler Cells to the Granule Cells of the Molecular Layer.

directly from the white matter; both of these are probably afferent routes by which impulses can reach the cerebellar cortex in general and the Purkinje cell in particular. The axon of the cell is probably efferent in function, transmitting impulses to the cerebro-spinal axis.

Cerebellar nuclei.—In the white matter of both the lateral and the mesial cerebellar lobes we find isolated masses of grey matter which give origin to very important bands of nerve-fibres. Thus in the centre of the lateral hemisphere lies a flask-shaped body—the dentate nucleus—closely resembling that found in the olivary body in the medulla. A large band of white fibres passes from it into the superior peduncle and later into the crus cerebri.

In the middle lobe, immediately above the fourth ventricle, lie a number of small nuclei, namely the nuclei emboliformis, globosus and fastigii. The latter is often called the roof nucleus and is of special importance as it is connected with fibres which pass downwards to arborise with the cells of Deiters' nucleus. This band of fibres is frequently called the vestibulo-spinal tract.

Connections of the Cerebellum.

The organ is connected to the mid-brain by the superior peduncle or processus ad cerebrum; to the pons by the middle peduncle or processus ad pontem; and to the medulla and spinal cord by the inferior or processus ad medullam. All the peduncles consist of medullated nerve-fibres, which convey impulses both to and from the cerebellum.

The **superior peduncle.**—Though the bulk of the fibres in this peduncle are derived from the dentate nucleus in the lateral cerebellar lobe, some appear to come from the cortex, more especially of the vermis. The fibres pass upwards and forwards under cover of the corpora quadrigemina into the tegmentum, where they decussate and form synapses in the tegmental grey matter, more especially with the cells of the red nucleus.

The **middle peduncle** connects the transverse fibre system of the pons with the lateral cerebellar hemisphere, though some of the constituent fibres seem to pass also to the grey matter of the vermis. Many of the fibres are apparently the axons of cells of the nuclei pontis, and may be considered to be afferent in function, while others seem to come from the cerebellar grey matter and

carry impulses both to the pyramidal and the tegmental regions of the pons and crus.

The **inferior peduncle** contains a very large number of fibres, derived partly from the postero-lateral ascending (cerebellar) tract of Flechsig and the restiform body, and partly from the arcuate system of the medulla and the cuneate and gracilis nuclei. All these fibres probably carry afferent impulses to the cerebellar cortex; on the other hand, we have some descending fibres which pass into the bulb and are found later both in the posterior longitudinal fasciculus and in the descending cerebellar tract of the spinal cord.

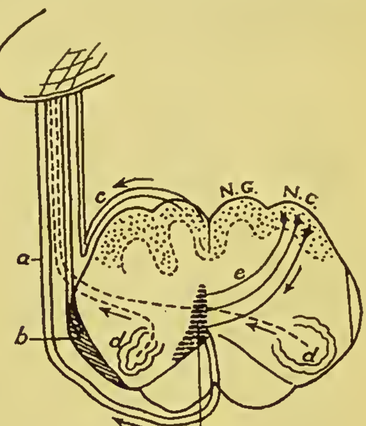

Fig. 434.—Diagram showing the Composition of the Restiform Body.

N.G., Nucleus gracilis; N.C., nucleus cuneatus; *a*, external arcuate fibres; *b*, direct cerebellar fibres; *c*, fibres from the nuclei gracilis and cuneatus; *d*, fibres from the olivary bodies; *e*, internal arcuate fibres.

The Cranial Nerves.

The **olfactory** or first cranial nerve.—The olfactory mechanism is somewhat peculiar, as it consists not only of an ordinary peripheral sense organ, comparable to the rod and cone layer of the retina, or the organ of Corti, but also of a specially developed outgrowth of cerebral substance—the olfactory lobe—which is connected on the one hand with the peripheral sense organ in the nasal mucous membrane, and on the other with the analytical centres in the brain.

The *olfactory cell* is essentially a bipolar nerve-cell with a well-defined oval nucleus and a peripheral and a central process. The former is rod-like and passes outwards to the free surface of the mucous membrane, where it ends in a number of short, stiff hairs which project slightly into the nasal cavity. The central process is very slender and somewhat varicose; it passes upwards into the olfactory bulb and ends in one of the glomeruli found in the lower part of that area.

The *olfactory bulb* can be roughly divided into three zones:—a superficial, consisting of nerve-fibres passing backwards from the bulb to the cerebrum in the olfactory tract; an intermediate, containing a large number of nerve-cells, called the mitral cells; and an inferior, or layer of olfactory glomeruli.

The mitral cells, large in size and very characteristic in shape, have several dendritic processes, which pass down to assist in the formation of the olfactory glomeruli, and a single axon which runs backwards towards the cerebrum.

The olfactory glomeruli consist of interlacements of nerve-fibrillæ derived from the arborescences of the central processes of the olfactory cells and the dendrites of the mitral cells. When stained by Golgi's method they are peculiarly distinct.

Fig. 435.—Olfactory Mechanism.

a, Olfactory cells, with their peripheral and central processes; *b*, olfactory glomeruli; *c*, mitral cells; *d*, axons of mitral cells passing backwards to the cerebrum; *e*, superficial cells.

The exact distribution of the olfactory fibres in the cerebrum has not been at all clearly defined. As the olfactory tract passes over the under surface of the brain it divides into two roots — an external and internal; the former runs directly back to the uncal region (regio olfactorius) on the same side, while the inner root passes into the anterior commissure and enters the anterior portion of the contra-lateral gyrus fornicatus. Though the bulk of the fibres appear to end in the olfactory region in the gyrus hippocampi, others sweep round by the fornix to the corpora mammillaria and then through the ascending fibres of Vicq d' Azyr to the optic thalamus and probably to the subthalamic region. Section of the nerve produces anosmia or loss of olfactory sensation.

The **optic** or second cranial nerve.—As the peripheral sense organ of vision has been already described fully in the section dealing with the histology of the eyeball ("Retina," page 577), we shall merely discuss here the chief connections of the various fibres contained in the optic nerves and tracts. The majority of the optic fibres are afferent and are derived from the ganglion cells lying in the second layer of the retina. This can be readily

demonstrated by excising an eyeball, when the great bulk of the fibres at once degenerate. The two optic nerves converge as they pass towards the cerebrum until they meet at the optic chiasma, where in the great majority of animals there is a partial decussation of the fibres. As a general rule, it is only the fibres that supply the inner halves of the two retinæ which decussate, the outer or temporal fibres sweeping backwards to the basal ganglia on the same side of the brain.

The chiasma also contains a number of fibres which are not directly connected with the visual apparatus, such as those in the bundle of Gudden, which pass between the two internal geniculate bodies. The optic tracts extend between the optic chiasma in front and the basal ganglia behind, more especially the external geniculate and the anterior quadrigeminal bodies, and in some animals the pulvinar of the optic thalamus. In these areas the fibres break up into terminal arborescences, forming synapses with cells which act as relay stations and transmit the visual impulses to other parts of the central nervous system.

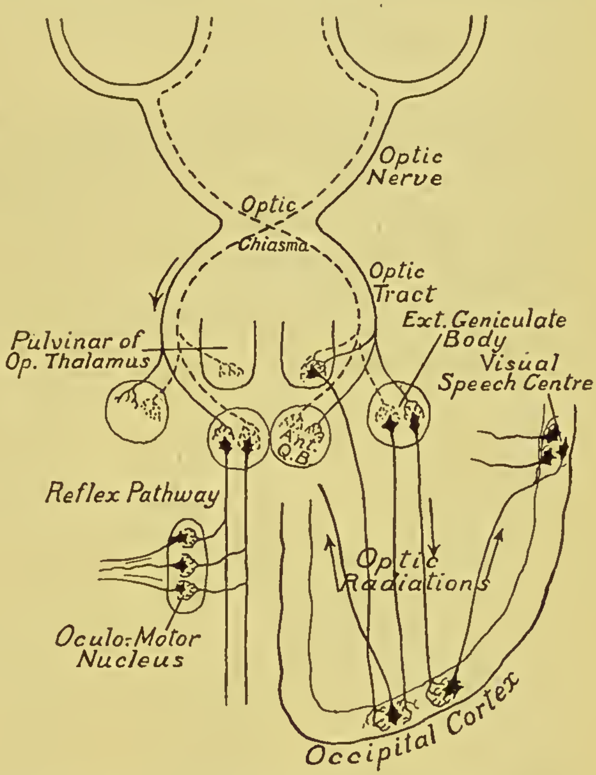

Fig. 436.—Scheme of the Distribution of the Visual Fibres.

Of the three areas, the external geniculate body seems to be most closely associated with the perception or analysis of visual sensation, as the axons of the cells in that area pass directly backwards to the occipital cortex, which, as we shall see later, appears to be especially concerned in vision. These fibres are frequently incorporated with others derived from the pulvinar of the optic thalamus, forming a number of well-marked nerve-bundles, called the optic radiations of Gratiolet.

The axons of the cells in the anterior quadrigeminal bodies, on the other hand, pass down into the tegmentum (probably in the ventral longitudinal fasciculus) and pass to the nuclei of the ocular nerves, more especially of the third, forming a path by which afferent visual impulses can reach the oculomotor centre and reflexly induce such movements of the ciliary muscle (accommodation), the sphincter pupillæ, or the extrinsic muscles of the eyeball, as may be required.

Effects of Lesions of the Optic Mechanism.—Leaving out of consideration lesions of the peripheral organ or retina, we may destroy the continuity of the visual pathway either by section of the optic nerve, chiasma or tract, or by ablation of grey matter of either the basal ganglia or the occipital lobe.

Extirpation of the eyeball or section of the optic nerve necessarily leads to complete blindness in that eye; in addition, however, we get degenerative changes in the basal ganglia, from which many of the connections of the optic fibres can be ascertained. If the operation be performed in an animal immediately after birth (before vision is established) it is found that the anterior quadrigeminal and the external geniculate bodies, and to a lesser extent the posterior part of the optic thalamus, either remain imperfectly developed or indeed atrophy. As neither the internal geniculate nor the posterior quadrigeminal bodies are affected we may infer that they are not directly connected with the visual mechanism.

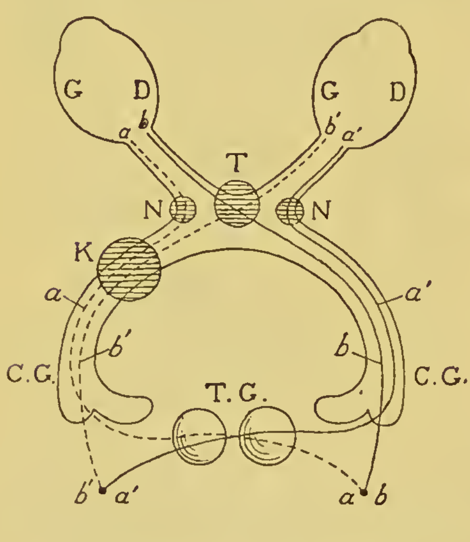

Fig. 437.—Diagram of Decussation of Optic Tracts.

T, Semi-decussation in chiasma; *T.G.*, fibres passing through the corpora quadrigemina; *aa′*, temporal fibres; *bb′*, nasal fibres; *C.G.*, corpora geniculata.

From the decussation of the nasal fibres of the optic nerves at the chiasma, extirpation of one eyeball leads to degeneration on both sides of the cerebrum. The commissure of Gudden is not affected, as it passes between the two internal geniculate bodies, which are not included in the degenerative process.

A lesion of the **optic chiasma** (as the presence of a tumour) leads to a degeneration of the nasal fibres which decussate in this area, so that we get a break in the pathway between the nasal portion of the retina on the one side and the contra-lateral basal ganglia; as a result, there is an inability to perceive dextro-lateral objects with the right eye and sinistro-lateral ones with the left eye (heteronymous hemianopsia) (Fig. 437, lesion at T).

Lesions of the **optic tract.**—A lesion in this position leads necessarily to blindness in the corresponding halves of the two retinæ, so that there is a similar blindness in each eye to external objects, or homonymous hemianopsia (Fig. 437, lesion at K).

Ablation of the **occipital cortex.**—As this will be considered in some detail in the section dealing with the cerebral cortex, we shall merely mention here the degenerative effects which follow the operation, as it tends to corroborate the deduction drawn from the previous experiment of extirpation of the eyeball. After removal of the occipital cortex there is a primary degeneration of the radiating system of fibres connecting that region with the basal ganglia, and somewhat later an atrophy of the three ganglia we have so frequently mentioned, namely, the external geniculate and anterior quadrigeminal bodies and the pulvinar of the optic thalamus. The connection between the cortex and the quadrigeminal bodies is extremely well marked in some of the lower animals, but is comparatively slight in man. Flechsig has also demonstrated by the medullation method that the chief connection is undoubtedly that between the external geniculate body and the cortex, and, further, that the pulvinar does not seem to be of very great importance, as there does not appear to be any distinct band between it and the cortex. In addition to the centripetal or afferent fibres, which undoubtedly form the bulk of the optic radiations, there are a number of efferent fibres which pass primarily to the anterior quadrigeminal body, but are probably continued later to the nucleus of the third nerve in the crus.

The **oculomotor** or third cranial nerve.—The nerve arises from a group of small nuclei situated in the crus cerebri, immediately in front of the aqueduct of Sylvius, and extending upwards as far as the hinder part of the third ventricle (Fig. 438).

There are two distinct groups of nuclei, an antero-median and a postero-lateral, the former containing small nerve-cells, and the latter composed of several small nuclei containing large cells. Stimulation of the various parts of the centre results in the production of definite movements. Thus excitation of the anterior end of the nucleus induces movements of the ciliary

muscle, of the middle portion movements of the pupil, and of the hinder part contraction of the extrinsic muscles of the eyeball, namely, the inferior and superior rectus, the levator palpebræ superioris, the inferior rectus, and the inferior oblique. On their way through the crus the fibres pass through the substance of the red nucleus, though they do not seem to have any connections with its cells.

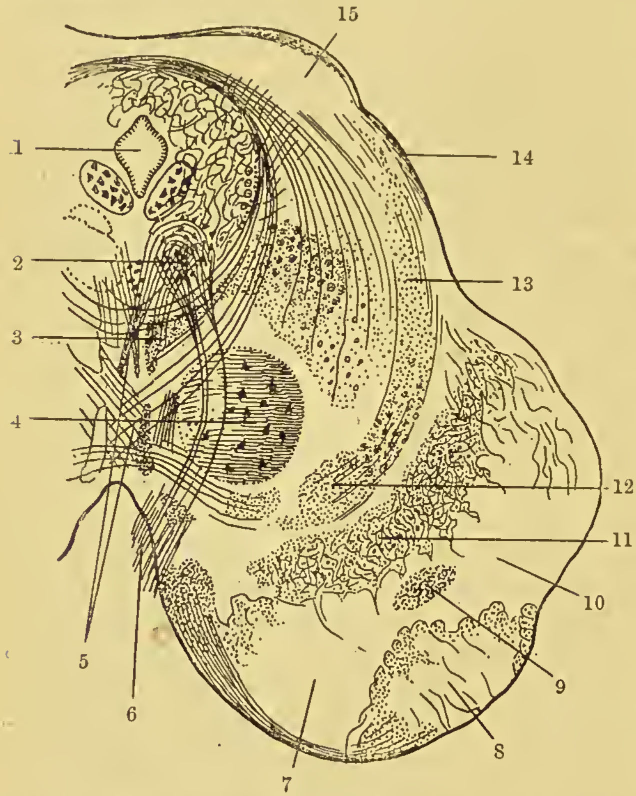

Fig. 438.—Transverse Section through the Upper Part of the Crus.

1, Aqueduct of Sylvius; 2, third motor nucleus; 3, posterior longitudinal fascia; 4, red nucleus; 5, fountain decussations; 6, third nerve; 7, frontal projection system; 8, pyramidal projection system; 9, caudate projection system; 10, temporal projection system; 11, substantia nigra; 12, median fillet; 13, lateral fillet; 14, brachium; 15, anterior quadrigeminal body.

Connections of the nucleus.—The most interesting and probably the most important connection of the oculomotor nucleus is that with the anterior quadrigeminal body, as it brings the afferent pathway of vision into touch with the reflex muscular mechanism of the eyeball. This connection is probably established through the ventral longitudinal fasciculus, a band of fibres coming from cells in the grey matter of the anterior corpora quadrigemina and passing down into the crus, where it later becomes incorporated with the posterior longitudinal bundle. The hinder part of the third nucleus is also connected (again through the posterior longitudinal bundle) with the contra-lateral sixth nucleus, so that we can secure a co-ordinate movement of the external rectus of the one eye (sixth nerve) with the internal rectus of the other (third), as when both eyes require to be rotated outwards as in the perception of a lateral object (conjugate

deviation). As the posterior bundle is closely connected with Deiter's nucleus, and the latter with the cerebellum, a pathway is thus established by which cerebellar influence can be brought to bear on the ocular mechanism, and by which necessary co-ordination of muscles can be secured. The posterior end of the third nucleus is also very closely related to the upper part of the motor nucleus of the fifth nerve, or, as it is generally called, its ascending root.

Lesions of the third nerve.—Section of the nerve leads to the following results:—(1) Paralysis of the ciliary muscle, and consequently a failure in the accommodative mechanism. (2) Paralysis of the sphincter pupillæ, with resultant dilatation of the pupil from the unopposed action of the sympathetic filaments supplying the dilator pupillæ muscle. (3) Paralysis of the levator palpebræ superioris, so that there is a drooping of the upper eyelid or ptosis. (4) Paralysis of some of the extrinsic muscles of the eyeball. namely, the superior and internal recti, the inferior rectus, and the inferior oblique. As a result, the unopposed action of the external rectus rotates the eyeball outwards—external strabismus or squint. (5) Diplopia or double vision.

While the third nucleus is generally stimulated reflexly by the reception of afferent impulses through the optic nerve and anterior quadrigeminal body, it can also be affected directly, as by the administration of certain drugs, such as opium, &c.

The **trochlearis** or fourth cranial nerve.—The nucleus is situated almost immediately below the third, in front of the aqueduct of Sylvius, and practically opposite the inferior quadrigeminal body. The nucleus is connected by the posterior longitudinal bundle with the other ocular nuclei, namely the third and the sixth. After leaving the nuclei the nerves sweep backwards into the valve of Vieussens, where they decussate before emerging at the side of the crus. This is the only cranial nerve which decussates before emergence. The nerve supplies the superior oblique muscle of the eyeball, so that if it be divided the pupil can no longer be rotated downwards and outwards. There is also diplopia if this movement be attempted from the unopposed action of the inferior rectus.

The **trigeminal** or fifth cranial nerve.—Unlike the third and fourth and sixth nerves, which contain only efferent fibres, the trigeminal is partly motor and partly sensory.

The centripetal fibres, as in all the cranial nerves, are derived from an external source, namely, the bipolar cells in the Gasserian

ganglion, in exactly the same fashion as the afferent fibres of the posterior nerve-roots of the spinal nerves are formed from the cells of the spinal ganglia. The peripheral fibre passes outwards along the nerve to the sensory surfaces supplied by the nerve, such as the cheek, lips, gums, or tongue, while the central process runs into the bulb and almost immediately bifurcates, one branch passing for a short distance upwards and terminating in synapses in a chief sensory nucleus, situated externally to the motor one, while the other travels down the cerebro-spinal axis in a bundle of fibres, forming the so-called descending or sensory root of the nerve and terminating in synapses with cells situated either in little islets among the fibres themselves or in their immediate vicinity. This descending root is situated immediately external to the substantia gelatinosa of Rolando, and it would appear as if many of the fibres pass into the latter and form synapses with the nerve-cells there. The efferent fibres are derived chiefly from two sources, namely, a rounded mass of grey matter situated in the upper part of the pons, near the edge of the fourth ventricle, and called the principal motor nucleus, and also from a chain of large cells extending upwards as far as the posterior end of the nucleus of the third nerve and forming the ascending or motor root of the nerve.

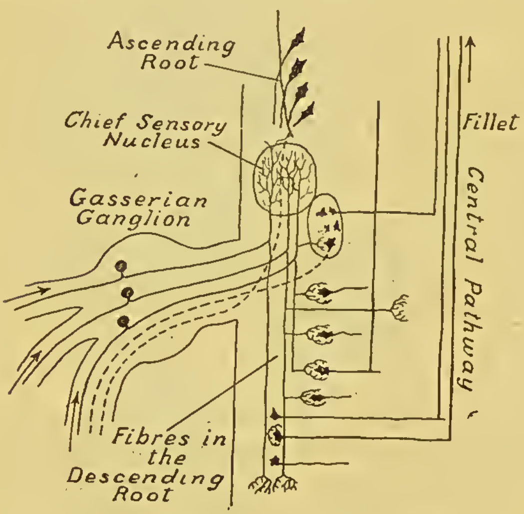

Fig. 439.—Scheme of Fifth Nerve.

Functions of the fifth nerve.—The motor fibres pass directly into the third or inferior maxillary division of the nerve and supply the muscles concerned more especially with the movements of mastication, such as the temporals, the masseter, and the pterygoids. It also supplies the tensor tympani and the tensor palati.

The sensory fibres are very widely distributed to the skin and mucous surfaces of the mouth and the lower part of the nose. It supplies the skin of the temples and face, the conjunctival surface of the eyeball, the lips, teeth, gums, palate and tongue.

Irritation of the nerve, as from chills, a lowered state of the health, or the presence of some more definite irritant, such as a decayed tooth, may set up an extremely painful condition—neuralgia—which may either be confined to a single branch or may affect the whole distribution of the nerve.

The **abducens** or sixth cranial nerve.—The fibres of this purely efferent nerve are derived from an oval mass of grey matter lying close to the mesial line in the pontine portion of the floor of the fourth ventricle. Like the cells of the third and fourth nuclei, those of the sixth are connected by the fibres of the posterior longitudinal fasciculus with Deiter's nucleus and the cerebellar cortex. The nerve supplies the external rectus muscle of the eyeball; if it be divided, internal strabismus results from the unopposed action of the internal rectus muscle, so that, as in division of the third nerve, we get diplopia or double vision.

Fig. 440.—Transverse Section through Pons at the Level of the Vestibular Root.

1, Restiform body; 2, accessory nucleus; 3, vestibular division of eighth nerve; 4, trapezium; 5, dorsal nucleus.

The **facial** or seventh cranial nerve.—The nerve contains both afferent and efferent fibres. The afferent are derived from cells in the geniculate ganglion, which send their central processes into the nervus intermedius of Wrisberg, between the seventh and eighth nerves. The fibres pass chiefly to the region of the glosso-pharyngeal nucleus. The efferent or motor fibres come from a group of cells situated slightly behind the nucleus of the sixth, and somewhat external to it (Fig. 440). The axons

sweep backwards towards the floor of the ventricle, and curl round the nucleus of the abducens; they then pass ventrally through the substance of the pons, between the descending root of the fifth nerve and the substantia gelatinosa on the one hand, and its own nucleus of origin on the other.

Functions.—The efferent fibres are chiefly motor to the expression muscles of the face and the stapedius in the middle ear; the nerve, however, contains also some secretory fibres which pass through the chorda tympani to the submaxillary and sublingual glands. The afferent fibres convey sensations of special taste from the anterior two-thirds of the tongue, most probably to the ninth nucleus.

Paralysis of the nerve is of fairly frequent occurrence. The lesion may take place either in the ear as the nerve passes through the internal auditory or the Fallopian canal, or in the face after it has emerged from the stylo-mastoid foramen. In the first situation the cause is generally referable to septic disease of the middle ear, and the paralysis includes the branches which are given off in that region, more especially the nerve to the stapedius and the chorda tympani. As a result we get not only the ordinary paralysis of the expression muscles of the face, but also a marked interference with the perception of flavours (chorda paralysis) and an inability to modify the intensity of loud sounds, from the affection of the stapedius. In the peripheral paralysis all the branches of the nerve are involved. The face on the affected side is immobile, and can neither be moved at will nor participate in any emotional movement. The skin is smooth and the natural wrinkles are effaced, a point particularly noticeable on the forehead in elderly persons. The eye cannot be closed, the lower lid droops and the eye waters. On the affected side the angle of the mouth is lowered, and in drinking the lips are not kept in close apposition to the glass, so that the liquid is apt to run out. In smiling or laughing the contrast is most striking, as the affected side does not move, which gives a curious unequal appearance to the two sides of the face (Osler).

The **auditory** or eighth cranial nerve.—This purely sensory nerve consists of two great divisions, the vestibular and the cochlear; the first transmits impulses from the semicircular canals to the medulla and the cerebellum, and plays a very important part in the complex mechanism underlying the processes of co-ordination and equilibration, while the cochlear is entirely concerned in the conduction of auditory impulses. In Fig. 414 it will be seen that the two roots of the nerve pass through the

medulla on either side of the restiform body. The vestibular root is anterior and somewhat mesial, while the cochlear is postero-external. In the triangle formed by the anterior rounded surface of the restiform behind and the two converging roots of the nerve in front lies a small mass of grey matter, called the accessory nucleus of the auditory nerve.

Connections of the vestibular root.—If the ventral root be traced backwards into the medulla it will be seen that the bulk of the fibres enter a large mass of grey matter lying internal to the restiform body and occupying a large part of the floor of the ventricle, and called the principal nucleus of the nerve. In this nucleus the fibres bifurcate, one set of fibres passing backwards to enter the cerebellum and to terminate there in synapses in the grey matter of the roof nuclei, whilst other fibres pass to synapses in the nuclei of Deiters and Betcherew. The descending branches pass down the medulla and synapse widely in its lower levels.

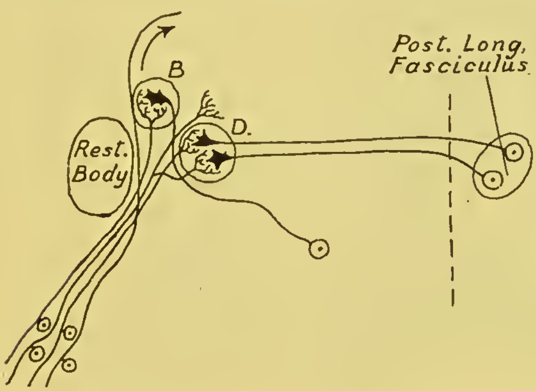

Fig. 441.—Simple Scheme of the Distribution of the Vestibular Fibres.

As Deiters' nucleus is one of the most important cell stations in the central nervous system, we must consider it in some little detail. It contains a large number of cells which send their axons into the posterior longitudinal fasciculus, where they bifurcate, one set of branches passing upwards in that bundle through the pons and crus to terminate in the subthalamic region. As they pass up they have numerous synapses with the groups of cells in their immediate vicinity, and more especially with the cells of the third, fourth and sixth cranial nuclei. The descending fibres assist in the formation of the descending cerebellar or vestibulo-spinal tract and end in arborescences in the ventral cornua of the spinal cord. As the cells in Deiters' nucleus synapse extensively with cerebellar fibres, it will be apparent that we have in this system a pathway by which cerebellar impulses can be transmitted to the different parts of the cerebro-spinal axis.

Connections of the cochlear root.—The fibres of the cochlear root can be divided into two groups—an external bundle which passes over the outer aspect of the restiform body and forms the

tuberculum acusticum, and an inner which passes directly into the accessory nucleus of the nerve. In some animals the tuberculum acusticum is very well developed ; it contains a number of nerve-cells which send their axons transversely across the floor of the fourth ventricle (the striæ acusticæ) to the other side, when they pass deeply into the substance of the pons and enter the lateral fillet, up which they pass as far as the inferior quadrigeminal body. The axons of the cells in the accessory nucleus pass transversely across the pons, forming the trapezium, and form synapses with cells in a group of lateral nuclei on the other side; some of the fibres pass directly, however, into the lateral fillet and run upwards in that tract to the mid-brain (Fig. 443).

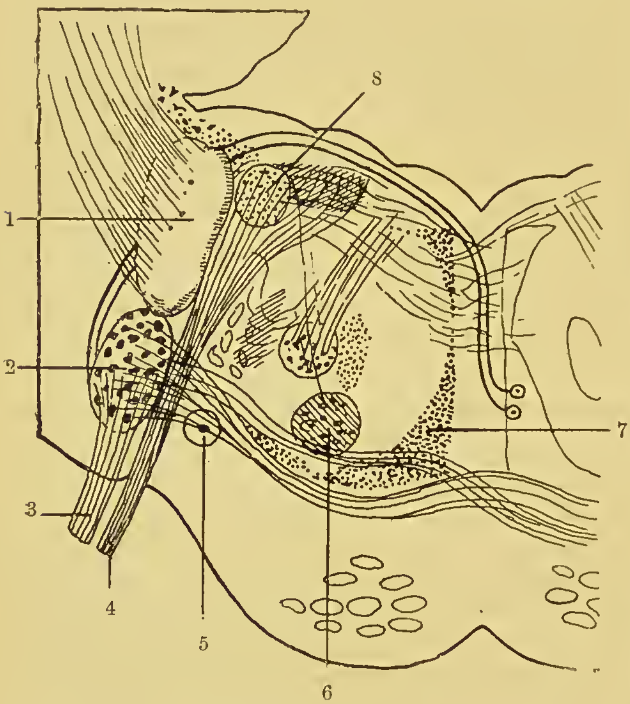

Fig. 442.—Transverse Section through Pons.

1, Restiform body: 2, accessory nucleus; 3, cochlear root; 4, vestibular root; 5, trapezium; 6, superior olive; 7, fillet; 8, Deiter's nucleus.

Functions of the cochlear and the vestibular roots.—The cochlear root is apparently concerned with the transmission of auditory impulses, primarily to the medulla and later through the lateral fillet to the inferior quadrigeminal body and the tegmental region. Flechsig has shown, further, that these areas are in turn connected with the internal geniculate bodies and the grey matter of the upper temporo-sphenoidal lobe.

The vestibular root, on the other hand, conveys impulses either directly to the cerebellum or by means of Deiters' nucleus brings the cerebellum and the vestibular root fibres into connection with the posterior longitudinal fasciculus and the regions traversed by the fibres of that bundle. It is apparently the chief root by which centripetal impulses pass to the cerebellum.

The **glossopharyngeal** or ninth cranial nerve.—The ninth nerve contains both afferent and efferent fibres. The efferent are derived from the cells of a special nucleus, which is probably an upward extension of the nucleus ambiguus, or motor nucleus of the vagus. The afferent are the processes of cells in the petrosal and jugular ganglia of the nerve. In accordance with the general plan, the fibres bifurcate after entering the medulla, the superior branches passing obliquely backwards to a nucleus lying immediately above

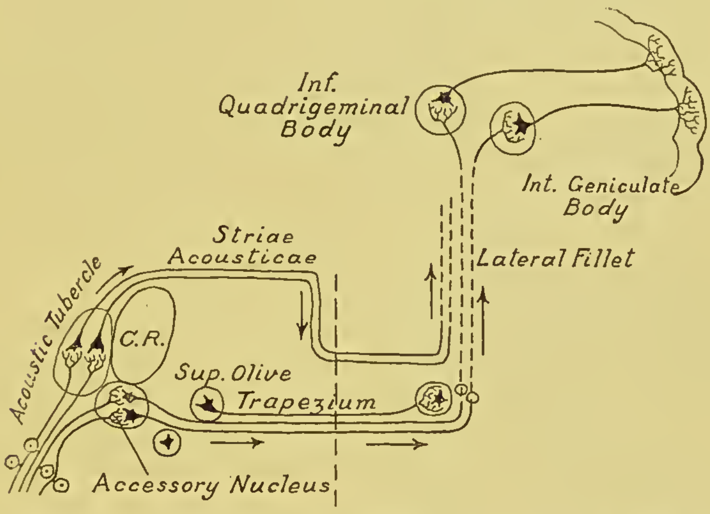

Fig. 443.—Scheme of the Distribution of the Fibres of the Cochlear Root.

the dorsal or sensory nucleus of the vagus, while the descending branches enter a well-marked bundle of fibres called the fasciculus solitarius, which passes down into the lower levels of the bulb, where the fibres end in synapses with cells lying in a mass of grey matter immediately internal to it, though in some instances the cells seem to lie among the fibres, or are arranged in small islet-like masses.

Functions.—The motor fibres supply certain muscles of the pharynx, such as the stylo-pharyngeus and the middle constrictor, and probably some of the palatal muscles. It also sends secretory fibres to the parotid gland. The afferent fibres supply the posterior third of the tongue with both ordinary and special sensation, and also the pharynx and the palatal folds. It will also be remembered that the nerve plays a very important part in the respiratory mechanism, as stimulation of the terminals of

the nerve leads to a temporary cessation of respiration, as, for example, in the act of swallowing.

The **pneumogastric, vagus**, or tenth cranial nerve.—Like the ninth, with which it is very closely associated, the vagus contains both afferent and efferent fibres. The efferent are chiefly derived from cells in the accessory or motor nucleus, generally called the nucleus ambiguus, though a certain number of the fibres seem also to be derived from cells situated in the upper or bulbar nucleus of the spinal accessory, which merges insensibly into that of the vagus. The afferent fibres are the processes of cells situated in the root and trunk ganglia of the nerve; the central processes pass into the bulb, where they seem to run a course practically identical with the glossopharyngeal fibres, the upper branches of the axons passing directly backwards to the dorsal or sensory nucleus, while the descending ones pass into the fasciculus solitarius. The trunk of the nerve receives through the accession of the pars accessorius vagi a large number of motor and probably cardio-inhibitory fibres from the spinal accessory.

Functions.—As the vagus supplies practically the whole of the alimentary canal and the glands, &c., developed in connection with it, a detailed description of its functions would hardly be possible here, more especially as they have already been considered in the sections dealing with the different areas. We shall, therefore, merely summarise the more important functions of the nerve. In the first place it supplies motor and sensory fibres to part of the pharynx, the œsophagus, the stomach and bowel, and secreto-motor and secreto-inhibitory fibres to the stomach, pancreas and intestinal glands. Through its superior and inferior laryngeal branches it supplies sensory and motor branches to the larynx and trachea: it is motor to the muscular fibres of the bronchioles and sensory through its pulmonary branches to the general lung substance. It will also be remembered that the nerve contains some fibres which promote both inspiration and expiration. The cardiac fibres are partly afferent and partly efferent; the latter are inhibitory to the heart, and according to Gaskell anabolic.

Lesions of the nerve.—If both vagi be divided, death of the animal generally takes place in from a week to a fortnight. There is marked interference with the process of deglutition, so that swallowing may be either very difficult or impossible, and the animal rapidly emaciates. The heart quickens in speed but becomes very feeble, and if the myocardium be examined after death, even where one vagus has been alone divided, patches of degeneration can frequently be made out. Death is very

commonly due to the development of broncho-pneumonia, often of a septic character; this is often ascribed to a failure of nutrition of the pulmonary tissue through a loss of trophism due to section of the nerve; it is, however, more probable that it is due to the entrance of food particles into the lung from the anæsthesia and paralysis of the glottis which follow the lesion. The division of one vagus does not produce any very marked results, at least not of a permanent character. In disease the nucleus of origin of the nerve may be affected, generally conjointly with the nuclei of the ninth and eleventh nerves, the disease in consequence being known as glosso-labio-laryngeal paralysis. As a rule there is a marked affection of the pharyngeal muscles in addition. The results of section of the nerve will necessarily depend on the position of the lesion and the fibres consequently implicated.

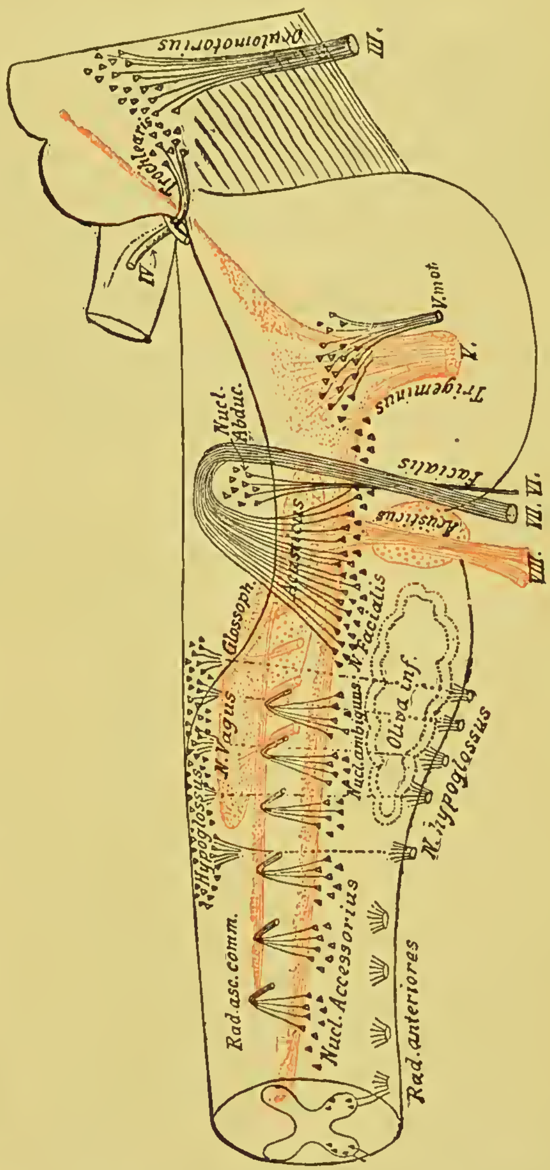

Fig. 444.—Nuclei of Origin of the Cranial Nerves.

The **spinal accessory** or eleventh cranial nerve.—Both the eleventh and twelfth nerves are purely efferent. The nerve has two nuclei of origin, a bulbar and a spinal; the former is incorporated with the hinder part of the nucleus of the vagus and sends its fibres to join that nerve, while the spinal nucleus extends down the cord as

far as the level of the fourth cervical root, and consists of a long chain of cells lying in the outer part of the ventral horn of the cord.

Functions.—The spinal portion of the nerve supplies the sterno-mastoid and trapezius muscles; while the medullary part joins the trunk of the vagus, supplying it with its motor fibres to the larynx.

The **hypoglossal** or twelfth cranial nerve.—The efferent fibres found in this nerve are derived from a mass of large cells situated at the side of the mesial line in the floor of the most posterior part of the fourth ventricle and immediately internal to the large combined nucleus of the ninth, tenth and eleventh nerves.

Function.—It is motor to the extrinsic and intrinsic muscles of the tongue.

Functions of the spinal cord.

These can be classified into:—(1) Conducting functions, (2) reflex functions, (3) automatic (?) functions, (4) trophic functions. Conduction may be either centrifugal or centripetal.

Centrifugal conduction.—The chief fasciculi which appear to carry efferent impulses are the pyramidal tracts from the cerebrum and the antero-lateral descending tracts from the cerebellum and medulla. The other tracts mentioned on page 674 we shall here omit, as we do not possess a sufficiency of evidence to enable us to state their function at all definitely.

Origin and course of the pyramidal fibres.—The fibres of the pedal projection system are chiefly the axons of the large pyramidal cells lying in the deeper parts of the pre-Rolandic gyri. As the fibres pass down through the corona radiata, or white matter, they converge until, in the region of the internal capsule, they form a solid pencil of fibres occupying the genu and the anterior two-thirds of the posterior limb. In the corona radiata they send off collaterals, some of which synapse in the contiguous grey matter, others with the cells in the grey nuclei, while the rest sweep through the corpus callosum to the contra-lateral hemisphere.

From the middle third of the internal capsule the fibres pass into the anterior portion of the crus, where they lie between the descending fibres of the fronto-pontine and the temporo-pontine projection systems (Fig. 417). In the pons the mass becomes broken up into fasciculi by the presence of the transverse fibres, and here the volume of the tract becomes very considerably reduced, as a number of the fibres pass to the nuclei pontis and the root cells of the cranial nerves. In the upper part of the medulla they are again collected into a single large bundle, the pyramid,

but in the lower part of the same region the bulk of the fibres

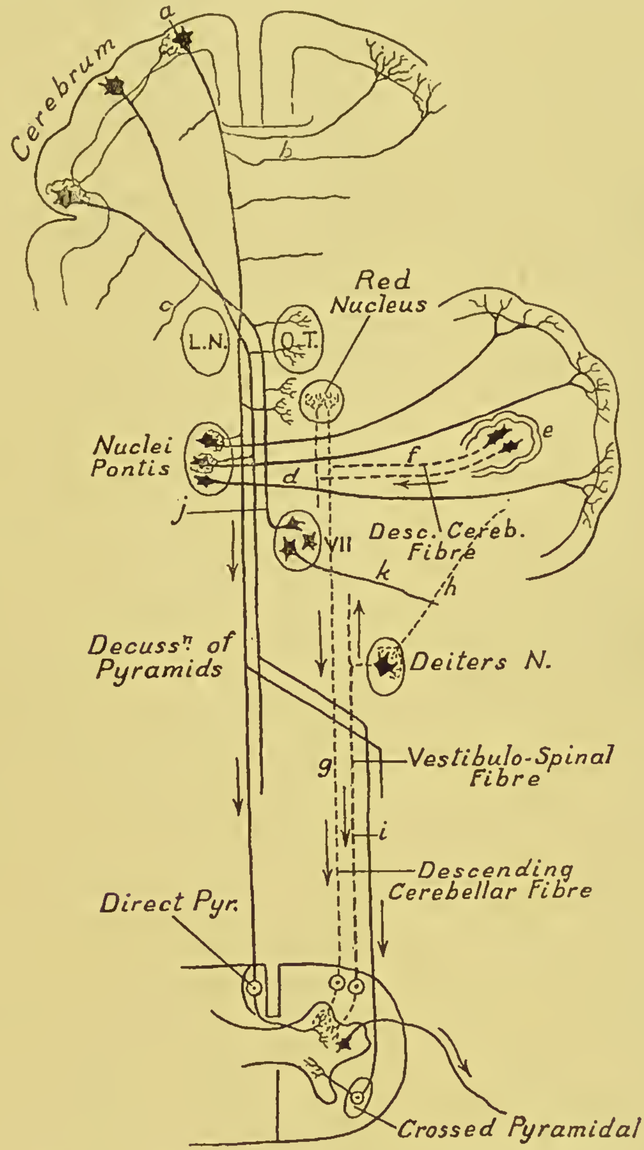

Fig. 445.—Scheme of the Descending Fibres from the Cortex, Mid-Brain and Cerebellum.

a, Cell in the leg area of motor cortex; *b*, collaterals from motor fibres; *L.N.*, lenticular nucleus; *O.T.*, optic thalamus; *d*, fibre linking the cerebellar cortex with the nuclei pontis; *e*, dentate nucleus; *f*, fibres which pass through the superior peduncle into the crus and there bifurcate into ascending branches passing upwards to the red nucleus and descending branches contained in the antero-lateral segment of the cord; *j*, motor fibres from the pre-Rolandic cortex passing to the contralateral seventh nucleus; *k*, fibres of the seventh nerve.

cross the median raphe, forming the decussation of the pyra-

mids, and enter the erossed pyramidal tract of the eord, down whieh they pass as far as their level of emergenee, when they leave the traet and enter the grey matter, terminating in synapses with cells situated ehiefly in the posterior horn (Fig. 403). Those fibres which did not cross in the medulla do so in the spinal cord, passing through the anterior or white eommissure to reach the eontra-lateral ventral horn. As they pass down the eord they give off eollaterals at every level, whieh pass into and ramify in the grey matter. The course of fibres of the pedal system ean readily be demonstrated by destroying a portion of the eerebral eortex—such as a part of the aseending frontal convolution — and noting the downward path of degeneration that results.

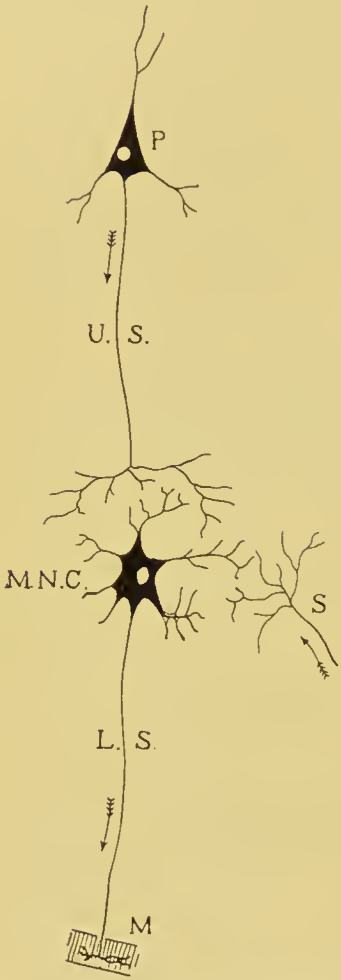

Fig. 446.—Diagram of Motor Nerve Path.

p, Pyramidal nerve-cell of cerebral cortex; *U.S.*, upper segment of nerve-fibre passing from it down the cord and arborising about the multipolar nerve-cell *M.N.C.*; *L.S.*, lower segment of motor fibre between spinal cell and muscle *M*; *S*, arborisation of sensory fibre of posterior root.

It will be seen that the degeneration extends from the site of the lesion down to the pyramidal tracts of the cord, proving that the descending fibre is derived from a cell in the eortieal area; this section of the motor nervous mechanism is very commonly called the first motor neuron. The seeond neuron extends from the anterior multipolar cell in the ventral horn of the cord to the nerve terminals in the muscles (Fig. 446).

Origin and course of the antero-lateral fibres. — They seem to be chiefly derived from the cells in Deiters' nucleus, though some of the fibres may come directly from the cerebellum. The fibres are collected into small bundles which pass down in the antero-lateral portion of the white matter of the cord among the ascending fibres of Gowers' tract. They end in the ventral horn in arboreseenees around the motor root cells.

Centripetal conduction.—The centripetal or sensory fibres enter the cord by the posterior nerve root and pass directly into the postero-external tract of Burdach and partly into the marginal tract of Lissauer. A few also pass directly into the grey matter and synapse with cells in the ventral horn and Clarke's vesicular column, thus completing in the first instance the reflex arcs at that level, and secondly through its connection with Clarke's cells, which may be considered relay stations on the spino-cerebellar pathway, a route by which ingoing impulses can reach the cerebellum. The main bundle of afferent fibres passes up the posterior columns as far as the medulla, where they end in synapses in the grey nuclear masses, the nuclei cuneatus and gracilis. As they pass up the posterior columns, however, they give off at all levels collaterals which enter the grey matter and synapse with cells in the anterior horn and Clarke's vesicular column. It will be obvious, therefore, that an ingoing nerve impulse not only passes upwards to the cerebrum, but is also transmitted by collaterals both across the cord to the anterior root cells, to excite reflex effects, and through the synapses with Clarke's cells to the cerebellum, there to assist in the complex nervous mechanism underlying the processes of co-ordination, equilibration, &c.

From the nuclei cuneatus and gracilis the impulses are transmitted upwards by the internal arciform fibres which cross the mesial line and later collect to form the lemniscus or fillet, which passes upwards through the pons and crus to terminate in the subthalamic region and the optic thalamus itself. A third relay of fibres passes between these areas and the cerebral cortex, completing the spino-cerebral path. We must now consider the route by which afferent impulses can pass from the cord to the cerebellum. The axons of the cells of Clarke's column pass into the lateral ascending tracts, more especially that of Flechsig. They then reach the cerebellar cortex by two distinct routes; thus while Flechsig's column can be traced directly into the inferior peduncle (Fig. 413) and later as far as the grey matter of the vermis, the fibres in Gowers' tract remain in the central cerebro-spinal axis as far as the entrance of the superior peduncle, through which they reach the cerebellar cortex. It is apparent, therefore, that the afferent nerve route is considerably more complex than the efferent, from the various directions in which the ingoing impulses require to travel in order to reach the areas associated with analysis, co-ordination, or reflexes, as may be required.

Our knowledge of the routes pursued by the afferent and efferent impulses has been chiefly derived from experiments involving a primary destruction of certain parts of the nervous system and a

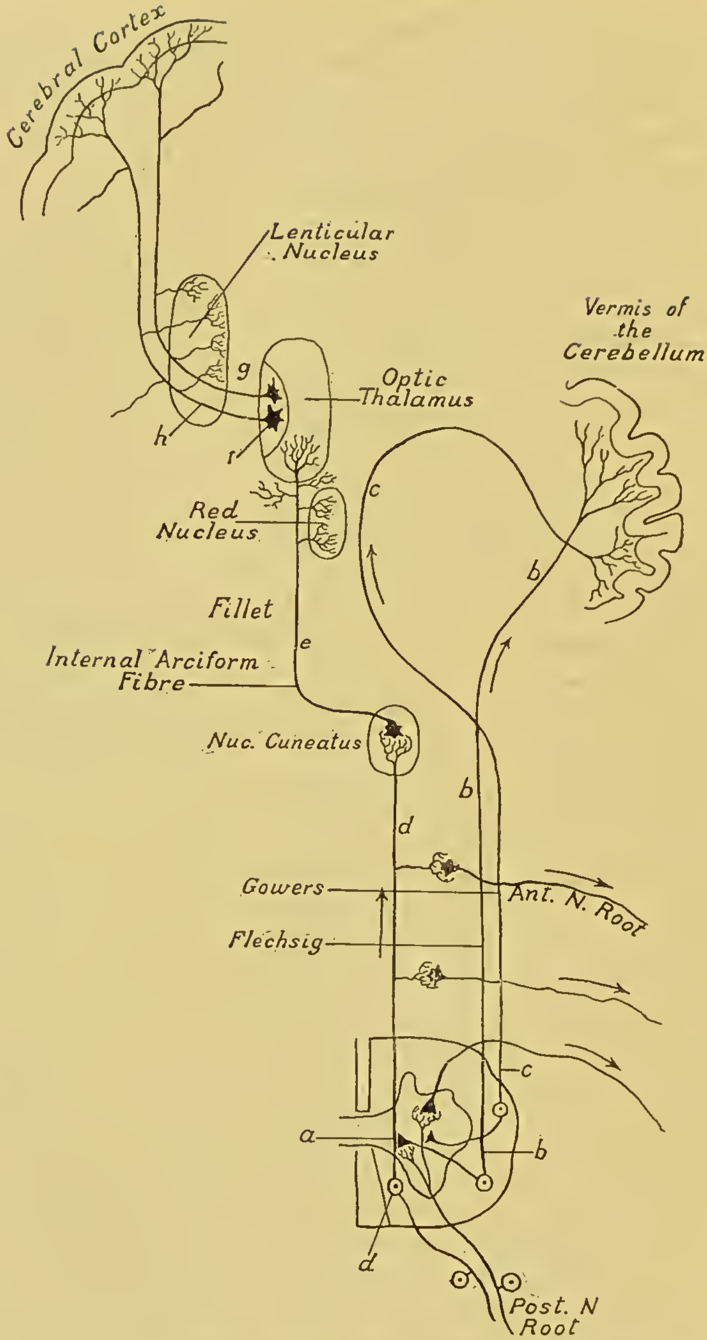

Fig. 447.—Scheme of the Ascending Fibres to the Cerebellum and Cerebrum.

a, Clarke's cell ; *b*, ascending cerebellar fibre (Gower's column) ; *c*, ascending cerebellar fibre (Flechsig's column) ; *d*, ascending central fibre in posterior column of Burdach ; *e*, fillet fibre ; *f*, cell station in optic thalamus ; *g*, internal capsule ; *h*, fibre linking *f* with the cerebral cortex.

later investigation of the paths of degeneration following the lesion. Thus after section of the posterior nerve roots we find a well marked zone of degeneration in the posterior columns, and if the lesion be situated in the lower portion of the cord this degeneration appears first in the postero-external column of Burdach and at higher levels in the internal tract of Goll. The degeneration is confined almost entirely to the homonymous side of the cord, so that it would appear that the great bulk of the afferent fibres is contained in the posterior columns on the same side, and that the decussation of the fibres takes place in the medulla. Certain experiments of Gotch and Horsley support to a certain extent these deductions. They estimated, by means of the capillary electrometer, the currents of action passing up the various parts of the spinal cord after stimulation of one of the posterior nerve roots at a lower level. They found that impulses passed up both the posterior and the lateral columns on both sides of the cord, though chiefly on the homonymous side. About 80 per cent. of the impulses pass upwards on the same side, and of this number about 60 per cent. lie in the posterior columns. Of the 20 per cent. which pass to the other side, fully 15 per cent. ascend in the dorsal tracts, leaving only a very small proportion of impulses to travel upwards in the contralateral lateral columns. Though on the whole these experiments confirm the deductions drawn from the Wallerian methods, one very important discrepancy will be at once noticed, namely the passage of a very considerable number of the fibres to the opposite side of the cord. Woroschilloff also showed that section of the contra-lateral portion of the cord produced a more marked interference with the transmission of sensory impulses than a similar lesion in the posterior columns, and consequently concluded that the afferent impulses passed to the cerebrum on the other side of the cord and chiefly in the lateral columns.

Semisection of the cord.—Weiss found that semisection of the cord in a dog produced immediate paralysis of both motion and sensation on the same side below the level of the lesion, but that more or less complete recovery took place after some time had elapsed, so that the dog was able to move about though single volitional movements of the muscles on the homonymous side did not take place. He later divided the other half of the cord at a higher level, and obtained complete paralysis of both motion and sensation, though this was again recovered from to a certain extent, showing that impulses can travel in zigzag fashion along the cord.

Schäfer and others have shown that somewhat similar effects

follow division of the cord in apes, though the motor and sensory paralysis seemed to be limited to the side of the lesion; there was also marked vasomotor paralysis on the homonymous side and an arrest in the secretion of the sweat. As in Weiss's experiment, the motor paralysis gradually passed off, so that after some weeks had elapsed it was difficult to determine any results of the lesion. Affections of the contra-lateral limb only appeared if the experimental lesion was not strictly confined to the one half of the cord. Pathological and clinical evidence unfortunately do not correspond at all closely with the deductions drawn from histological and experimental data. In pathological lesions involving definite areas of the cord, such as the dorsal columns, there may be very little interference with ordinary sensation; thus in locomotor ataxia, where the columns of Goll and Burdach may be completely sclerosed, ordinary tactile sensation may be unaffected while muscular and thermal sense may be either completely lost or greatly modified. Again, in myelitis, where one half of the cord is affected, symptoms are found on both sides of the body, the motor paralysis being generally most marked on the same side, and sensory on the opposite. In syringomyelia, a condition attended by degeneration of the grey matter surrounding the central canal of the spinal cord, there is not interference with ordinary tactile or muscular sensation, while, on the other hand, there are patches of local anæsthesia to pain and thermal sense. It is therefore supposed that the fibres conveying these special sensations synapse with nerve-cells situated in the grey matter in the immediate vicinity of the central canal, while the new neurons pass out into the white matter; for it has been shown that the grey substance may be completely hollowed out without producing pain and thermal anæsthesia in any other areas than in those corresponding to the site of the lesion. Gowers has recorded a case of apoplexy in the lateral columns where there was a complete loss of thermal and pain sensations on the opposite side without any interference of ordinary tactile sensation. The afferent sensations from the muscles, &c., (muscular sense) are generally supposed to be transmitted up the posterior columns, and we have already mentioned that in locomotor ataxia, where these columns are sclerosed, there is marked interference with this sensation.

It must also be remembered that we have a considerable number of tracts in the cord of a commissural or association character. These tracts vary greatly in length, the larger ones apparently connecting distant areas, such as the cervical with the lower lumbar segments, while shorter ones pass between more or

less contiguous parts. They are found in both the anterior and the lateral segments of the cord, more especially in the outer portion of the white matter. At all levels they send collaterals into the grey substance, which arborise around the various groups of nerve-cells. It will be apparent, therefore, that the destruction of any one tract, either by experiment or disease, will not necessarily prevent the passage of an impulse normally carried along that pathway, as it can be transmitted either by one of the association bands or in the grey matter by the synapses of the various cells with one another. The effect of complete section of the cord will necessarily vary with the position of the lesion; thus, in the higher cervical region a lesion will produce not only motor, vasomotor and sensory paralysis, but will also interfere with the respiratory fibres passing out in the phrenic and intercostal nerves, so that there will be complete cessation of respiration. At the same time there is a permanent constriction of the pupil from the unopposed action of the sphincter pupillæ supplied by the third nerve.

Lesions in the lumbar region, on the other hand, will interfere with the activity of the "centres" found in that area, chiefly those presiding over the rectal and vesical sphincters.

Conditions affecting the Activity of the Second Motor Neuron.

The activity of the anterior root cells is influenced by impulses transmitted along three distinct pathways:—(1) The pyramidal tracts which connect the cells with the kinæsthetic centres in the pre-Rolandic gyri. This is probably the avenue by which volitional impulses are transmitted to the second motor neuron. (2) The collaterals of the posterior or sensory root fibres; a pathway of extreme importance in the production of reflex action. (3) The antero-lateral descending tract of Löwenthal, by which inhibitory impulses pass from the cerebellum to the ventral cells to control the intensity of volitional or reflex movement, and thus to obtain co-ordinate or harmonious results.

The **reflex functions of the spinal cord.**—In many instances a motor act so obviously results from the entrance of some ingoing impulse that there is no possible difficulty in realising its reflex character. In many others, however, such as voluntary movements, the reflex element is subordinate to a psychical process, so that it may be more or less entirely overlooked. As we have already mentioned (page 662), the anterior or motor root cells are constantly maintained in a state of slight activity

by the reception of afferent impulses through the posterior or sensory nerve roots, and we find an exactly similar condition in the other parts of the central nervous system. Thus Sherrington has shown by an ingenious experiment that the activity of the Rolandic areas is dependent largely upon the reception of afferent stimuli; for if the posterior roots of the brachial plexus be divided a marked inability to execute any of the finer movements of the hands results, though they can still be produced by a direct excitation of the cortex.

Reflex actions may or may not be attended with consciousness; indeed, it may be said that in the purer types consciousness is absent.

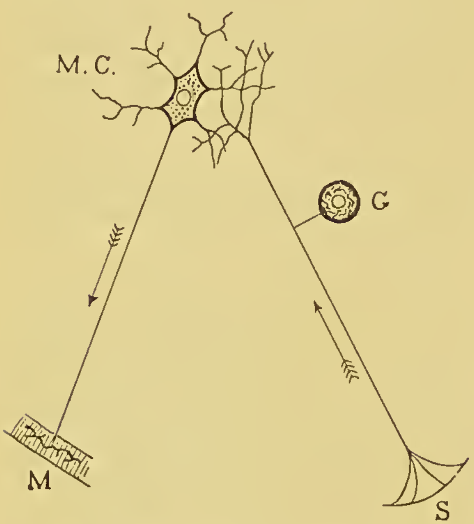

Fig. 448.—Reflex Action (Present View).

MC, Motor cell; *G*, ganglion; *M*, muscle; *S*, sensory surface.

Of these simple forms of reflex action we have many examples, such as the secretion of the digestive juices, and some of the movements of the various parts of the alimentary canal. The characters of reflexes can be studied very perfectly in the amphibia, where the relationship of the brain and the spinal cord is not so intimate as in mammals. If a decerebrated frog be suspended by a pin passed through its lower jaw, it will be found to respond to all types of stimulation. Thus if one leg be immersed in a weak acid solution, it will be seen that the muscles contract so that the limb is raised out of the fluid, or if a piece of paper soaked in acid be placed on the back, a limb will be lifted to remove it.

There is not much obvious change in the appearance of the frog, though the attitude is generally somewhat characteristic; though it has lost all volitional power it is still able to execute all types of co-ordinate movements on the reception of suitable stimuli, thus if placed in water it will swim, if pinched it will jump, if stroked it will croak. In other words it still possesses, and, as we shall see later, to an increased degree, the power of reacting to external stimulation, though it can no longer

execute voluntary movements, or go in search of food or exhibit any phenomena dependent on a volitional basis. It will also be observed that all the reflexes we have mentioned are of a distinctly purposive character and are not mere irregular and useless muscular movements due to a stimulation of groups of motor cells by ingoing impulses. The reflex path or arc, along which the afferent impulse is conveyed to the energising efferent cells, and the resultant impulse transmitted to the tissue, consists of:—(1) A sensory surface, such as skin or mucous membrane, (2) an afferent fibre derived from a ganglion cell on the posterior root, and terminating in a synapse with (3) an energising cell (or cells), such as those of the anterior horn, from which (4) an efferent fibre (or fibres) is given off which conveys the afferent impulse to the muscle or gland as the case may be (Fig. 448).

As the posterior root fibres give off collaterals at every level in the cord, which pass into and arborise in the grey matter, it will be apparent that an afferent impulse passing in at one posterior root may stimulate cells at every level, and thus produce widespread reflex results.

The extent or amount of the reflex action depends essentially on the intensity of the stimulus and the excitability of the central nervous system; thus after the injection of a dose of strychnine the reflexes become enormously exaggerated. If a very weak stimulus be applied to one limb, it will generally, though by no means always, be found that the muscles of that limb are thrown into contraction; as the stimulus is increased in strength convulsions appear, first in the contra-lateral limb and later throughout the rest of the body, from the radiation of the stimulus through the grey matter.

As might be expected, the integrity of the whole of the cord is not necessary for the performance of a reflex act, thus, for example, the whole of the hinder part of the spinal cord can be removed from the male frog during the "clasping" period without interfering with the contraction of the muscles of the fore limbs. Again, the upper part of the spinal cord can be affected without interfering with the activity of the centres in the lumbar segment.

Similar segmental reflexes can easily be demonstrated in the invertebrata. If a shark be beheaded the body will continue to move about in a perfectly co-ordinate manner (Howell), and a decapitated petromyzon will at once become active if placed in an irritant fluid such as a dilute acid.

In the higher mammals, and more especially in the apes and in man, the reflex functions of the cord are much less distinct. If the cord be divided the shock is generally so great as to com-

pletely arrest all reflex action, but if some time be allowed to elapse, so that this may pass away, a considerable number of reflexes, and more especially those concerned with the activity of the lumbar centres, reappear. In the dog recovery may be very pronounced.

Influence of the higher parts of the nervous system on spinal reflexes.—We have already seen that the reflexes of a decerebrated or "spinal" frog are much greater than those of the intact animal, and this is generally ascribed to the removal of descending inhibitory impulses which under normal conditions pass down the cord and regulate the extent of the reflex action. It has also been shown by Setschenow and others that stimulation of certain parts of the cerebro-spinal axis will produce these descending inhibitory impulses. If an injection of strychnine be given to a decerebrated frog, and the leg then allowed to fall into an acid, violent reflex spasms are induced. The application of a crystal of sodium chloride to the upper end of the spinal cord or the optic lobes, however, either arrests the convulsions or greatly modifies their intensity, apparently from the production of these powerful descending inhibitory impulses.

The reception by the central nervous system of a second sensory impression also greatly modifies the extent of reflex action. Thus the well-known Goltz phenomenon of cardiac inhibition, following mechanical stimulation of the intestine, does not occur if the leg be pinched at the same moment.

Again, the latent period of a reflex action becomes greatly increased if some other sensory nerve be simultaneously stimulated; indeed, it might be generally stated that stimulation of one part of the central nervous system seems to exert a depressant or inhibitory influence over the other parts (*cf.* Sherrington's experiment on Ocular Muscles, page 759). Some observers maintain that the brain—in the higher animals at least—is normally included in the reflex arc, and this suggestion certainly explains the practically complete loss of reflexes which follows section of the spinal cord in the higher animals; their subsequent reappearance being attributable to the passage of the afferent impressions directly across the cord to the ventral nerve cells as in the case of the amphibia.

Clinical reflexes.—As the very existence of reflected action depends on the integrity of the nervous pathway or reflex arc, it will be apparent that the phenomena are of great importance in the diagnosis of lesions of the central nervous system, and more especially those of the spinal cord.

Clinically, reflexes can be divided into two great classes, namely skin or superficial and tendinous or deep. In the first group, irritation of the skin, as by tickling, produces reflex muscular contraction: of these, the cremasteric, plantar and scapular reflexes are excellent examples.

The second group is of even greater clinical importance, though they can hardly be considered perfect examples of pure reflex action : of these, the most important is the knee-jerk.

If the one leg be balanced over the other and the foot allowed to hang so that the quadriceps extensor muscle is slightly stretched and a sharp tap then given to the tendon patellæ, the foot is at once jerked upwards by an involuntary contraction of the muscle. In many respects the phenomenon is identical with an ordinary reflex action, while in others it possesses distinct and sharp points of difference.

In all true reflex acts a certain time must necessarily elapse between the application of the stimulus and the appearance of the reflex motion or secretion as the case may be. During this reaction period, as it is called, the ingoing impulse is passing round the reflex arc and stimulating the various energising cells concerned in the action. The reaction time averages ·15 sec., though in types where the reflex pathway is very long or where psychical processes are involved, as in the "Dilemma," it may be greatly increased. In the knee-jerk the response is almost synchronous with the stimulation.

Again, it is not infrequently absent in healthy people, or in conditions such as atrophy of the extensor muscles, in which there appears to be no actual break in the reflex arc.

On the other hand, any lesion of either the peripheral nerve (as in neuritis) or the intra-spinal pathway (diseases of the spinal cord) at once prevents the development of the phenomenon.

If a decerebrated frog be suspended by a thread passed through the lower jaw, it will be observed that the limbs do not straighten out, as might be expected, but remain slightly flexed. On division of the motor nerves or destruction of the cord, this flexion at once disappears, showing that even in complete inactivity of the animal the muscles are constantly maintained in a condition of slight contraction or tone. This can only be due to either an automatic or a reflex energisation of the ventral nerve cells, and as the same relaxation follows section of the posterior or afferent nerve roots, the latter appears to be the more probable explanation.

Sherrington has shown that the motor nerves passing to the muscles contain a very large percentage of centripetal fibres, which are apparently connected with the curious terminals found in

muscle and described in the section dealing with muscular sensation. It is probable that ingoing impulses generated in these terminals are conveyed into the spinal cord and stimulate the ventral nerve cells, so that the muscles are maintained in this condition of tone.

Reciprocal action of muscles.—This is well exemplified in the case of the knee-jerk. If the flexor muscles or their nerve be divided, the tension or tone of the extensor becomes increased, so that the reflex is greatly exaggerated. Separation of the lower attachment of the flexor muscles, thus preventing any mechanical interference with the movements of the leg, leads to the same result, while, on the other hand, kneading of the separated muscle or stimulation of its nerve leads to an inhibition of the jerk.

In fine, the tonus of any muscle depends largely on the reception by its motor root cells of ingoing impulses transmitted from antagonistic groups of muscles.

Specialised reflex functions of the spinal cord.—Scattered throughout the cord we find areas which seem to be concerned with the performance of special reflex acts, such as the secretion of sweat, dilatation of the pupil, the maintenance of vascular tone and the tonic contraction of the sphincters governing the vesical and rectal apertures.

Thus, if the spinal cord be divided below the exit of the phrenic nerves the arterioles at once dilate, from section of the vaso-constrictor fibres; after some days, however, the vascular tone returns to nearly its original condition, from the activity of these spinal centres. This can be proved by slicing the cord away from above downwards, when the vessels again dilate. These subsidiary centres are affected by the same conditions which govern the medullary centre, namely, the reception of ingoing or sensory impulses and the condition of the blood (as in asphyxia), though the effects are not nearly as definite as in the case of the medullary centre. A very important group of "centres" lies in the lumbar portion of the cord, controlling the movements of the bowel and the bladder, and the genitalia.

If the spinal cord be divided in the lower thoracic region there is a temporary paralysis of the sphincters from the shock of the operation, which passes off in the course of a few days.

The recovery is practically complete (except in so far as consciousness is concerned), the tone of the sphincters being perfectly regained. Destruction of the lumbar region of the cord, however, produces a more complete and permanent paresis, the tonic con-

traction of the muscle being considerably affected. The animal still retains, however, powers of micturition and defæcation, though the act is generally incomplete. Gowers has pointed out that the introduction of a finger into the anal aperture sets up a continued and marked reflex contraction of the sphincter in cases where the lumbar centre is intact, while after ablation, the contraction, though fairly well marked at the moment of introduction (local spasm), soon becomes markedly feeble. The animal is still able, however, to defæcate at fairly regular intervals, so that the nervous mechanism must lie largely in the wall of the bowel itself. Local stimulation, such as pressure with the hand, will induce immediate micturition or defæcation, though the process is generally somewhat incomplete. Similarly, the introduction of balls of cotton wool into the rectum excite peristaltic contraction, so that they are at once expelled.

It is more difficult to decide whether there are any special centres presiding over the processes of parturition. Stimulation of the central end of the first sacral nerve excites reflex contraction of the uterus. Pregnancy can go on to full term in a bitch where the spinal cord has been divided in the mid-dorsal region, or even where the whole of the posterior part of the cord has been destroyed, and in these cases normal labour (of course unattended with pain) occurred at full term.

In the cervical portion of the cord a centre governing dilatation of the pupil has been described, called the cilio-spinal centre; it is more probable, however, that the fibres are really derived from a nucleus lying in the vicinity of the third ventricle and that they merely pass down through the pons and medulla into the cord on their way to the upper thoracic region, as they usually emerge in the upper three dorsal nerve roots.

Sherrington has shown that stimulation of the posterior nerve roots in this area of the cord does not induce any distinct change in the size of the pupil. It is quite possible, however, that the cilio-spinal cell-station is subsidiary to the cerebral centre.

Automatic functions of the spinal cord.—The term automatic is somewhat misleading, as the actions which were at one time considered to be automatic are essentially reflex, though of a sustained character, such as the action of the lumbar centres on the rectum and the bladder, &c. The continual energisation of the ventral nerve cells, which maintains the muscles in "tone," is another excellent example of this type of action.

Trophic functions of the cord.—In the section dealing with

the trophic functions of a nerve cell or its processes we saw that the division of the axon resulted in the atrophy of the separated portion. The muscle supplied by the nerve also undergoes marked degenerative change. In poliomyelitis anterior acuta or infantile atrophy, an acute disease affecting the anterior cornual cells, the muscles degenerate more or less completely.

The **functions of the medulla oblongata.**—Removal of the whole of the nervous system anterior to the bulb produces effects which closely resemble those found in a decerebrated animal.

The cardinal reflex actions associated with the processes of vaso-constriction and cardiac and respiratory action are not affected to any very great extent, though the respiration generally becomes somewhat less frequent and more prolonged.

The various reflex actions associated with the movements of the alimentary canal, such as swallowing, remain unchanged, and likewise those governing the secretion of the salivary and other glands. If the animal be placed on its back it will right itself, and if the bulb be suitably stimulated, as by the application of a crystal of sodium chloride, widespread muscular spasms are produced.

Ablation of the medulla is followed by the disappearance of most of these phenomena, thus respiration and cardiac action cease, while the arterioles dilate from the removal of vaso-constrictor influence.

The functions of the medulla may be summarised thus :—(1) It links the cord below with the pons varoli above, and conveys the various afferent and efferent fibres from the one to the other ; (2) it is the chief area where the various bands of fibres become rearranged and distributed to reach the different parts of the central nervous system ; (3) it contains a large number of groups of nerve cells—nuclei—more or less closely connected with the fibres contained in many of the cranial nerves (eighth, ninth, tenth, eleventh and twelfth) ; (4) it also contains nerve cells which appear to be directly concerned in the existence of a large number of reflex actions, some of them of the most vital importance, such as respiration, vaso-motion, and cardiac action, and others concerned with the secretions of the salivary and the lachrymal glands, the movements of the œsophagus, &c. The distribution of the fibres passing into the bulb has been already discussed in the section dealing with the structure of the area.

Functions of the pons and crus.—The pons and crus contain not only the great afferent and efferent pathways linking the

cerebrum and cerebellum with the spinal cord and bulb, but also the grey nuclei of origin of the sixth, seventh and part of the eighth cranial nerves, and in the crus those of the third and fourth. The nuclei pontis are cell stations where the cerebellar fibres synapse with those of the various cerebral projection systems.

In the upper part of the crus we have the red nucleus, which has not only important synapses with the ascending fibres, but also sends axons down through the pons and medulla into the cord, forming the rubro-spinal or pre-pyramidal tract of Monakow.

Lastly, the sensory fibres of two of the most important of the cranial nerves, viz., the fifth and the eighth, pass into the substance of the pons and become widely distributed throughout its grey matter.

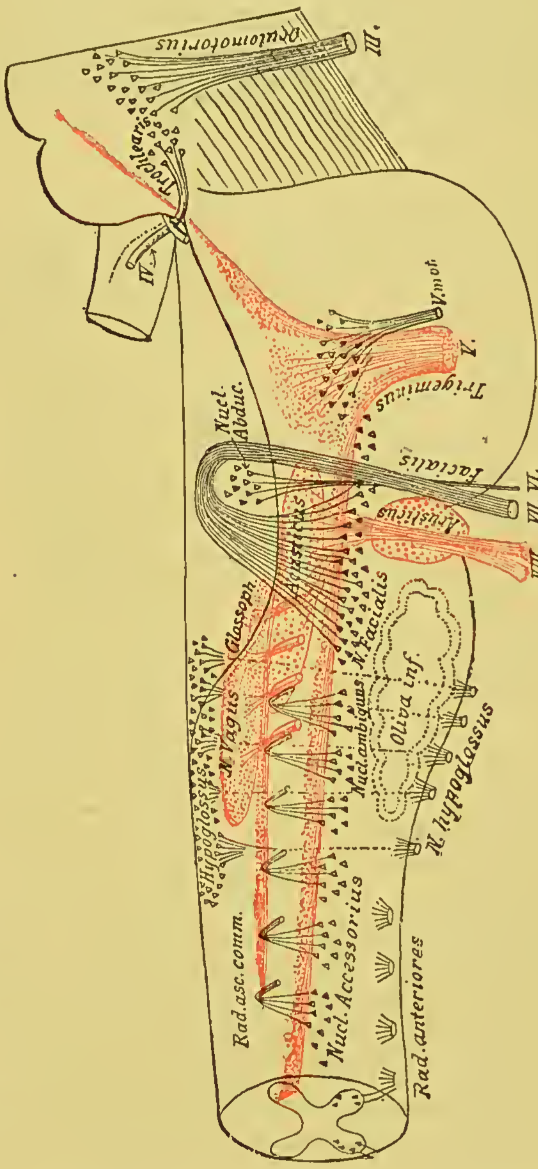

Fig. 449.—Nuclei of Origin of the Cranial Nerves.

Functions of the corpora quadrigemina and corpora geniculata.—From the connections of the inferior quadrigeminal bodies, by the lateral fillet, with the corpus trapezoideum in the pons and the nuclei of the cochlear division of the eighth nerve, it

might be immediately supposed that the nucleus was concerned with the reception or transmission of auditory impulses, and we have a considerable amount of experimental evidence in support of this belief. Thus, electrical stimulation of the inferior quadrigeminal bodies induces pricking of the ears, attempts at vocalisation, and other phenomena more or less closely associated with audition. Many of the fibres of the lateral fillet also pass to the internal

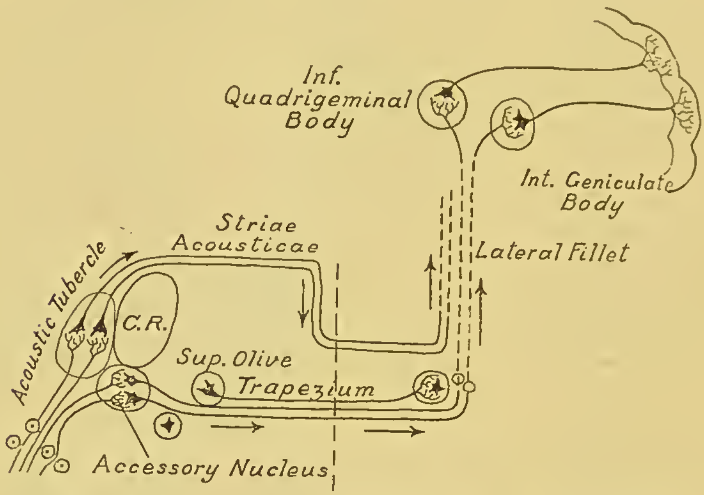

Fig. 450.—Scheme of the Distribution of the Fibres of the Cochlear Root.

geniculate body, and it is more than probable that these may also be considered important cell stations on the central auditory pathway.

The superior quadrigeminal bodies, on the other hand, seem to be almost entirely related to the visual pathway, and more especially to that portion concerned with the transmission of the ingoing impulses, not to the analytical or true visual centres in the occipital lobes, but to the centres of the third cranial nerve, which control the various mechanisms concerned in the reflex movements of the iris, the ciliary muscles and the majority of the extrinsic muscles of the eyeball.

The external geniculate body is a very important cell station in the central visual pathway (see "Optic Nerve," page 712).

Functions of the optic thalamus, subthalamic region, and the internal capsule.—Though our conception of the functions of

these areas rests chiefly on histological and clinical data, there is still a certain amount of evidence of an experimental character.

We have remarked that the thalamus and hypothalamus can be considered the upper end of the tegmental region of the crus, and that it contains the terminations of the mesial fillet and many of the fibres of the posterior longitudinal fasciculus, which can be considered the chief links joining the spinal cord with the basal ganglia.

The lateral nucleus of the thalamus, on the other hand, contains cells which send their axons laterally into the adjacent portion of the internal capsule, on their way to the lenticular nucleus and the cerebral cortex. It is evident, therefore, that the thalamus is a very important cell station on the sensory pathway.

Clinical Evidence.—Hæmorrhage into the internal capsule and the adjacent lenticular nucleus is a condition of frequent occurrence from the rupture of one or more of the small blood-vessels forming part of the lenticulo-striate or lenticulo-optic systems. The blood pours out among the fibres, and if in large amount tears up the tissue and destroys it, producing a more or less complete loss of function.

If the hæmorrhage be slight the fibres may be merely paralysed from pressure and a certain amount of recovery may take place. Small or localised hæmorrhages may produce very distinct and definite effects; thus, if the lesion be situated in the genu or anterior part of the posterior limb of the capsule the phenomena are chiefly those of muscular paralysis on the opposite side of the body (hemiplegia), while if the lesion be situated in the hinder part of the same area sensory phenomena (hemianæsthesia) predominate.

In most cases the hæmorrhage is fairly large, so that both types of symptoms are present. Lesions localised to the optic thalamus are of rare occurrence. In a well-known case, recorded by Hughlings Jackson, the chief symptoms recognised were an anæsthesia of the contra-lateral side of the body, associated with homonymous hemianopsia and impairment of the special senses of taste, smell and hearing. The paralysis of ordinary and special sensation can be attributed to the interference with the various sensory fibres which pass through the thalamus on their way to the occipital cortex, the gyrus hippocampi, &c. Ablation of the thalamus produces homonymous hemianopsia, similar to that following division of the optic tract, but there is also interference with other special senses, such as taste and smell. Large numbers of fibres seem also to pass to the thalamus from the cerebral cortex, and Mellus

has demonstrated that they are markedly smaller than the fibres of the pyramidal projection system.

Functions of the cerebellum.—In endeavouring to ascertain the functions of the organ, we will first consider the effects of destruction of part or whole of the cerebellum, and later note the evidence deducible from its anatomical connections with the cerebro-spinal axis and the effects of interference—experimental or pathological—with those pathways.

Ablation of the cerebellum.—The operation produces very distinct and characteristic phenomena, varying somewhat with the extent and position of the lesion.

In every case, however, it is found that there is no interference with psychical function or with analysis of special sensation, thus sight, smell, cutaneous sensation, appetite, &c., remain unchanged while the memory and intellect retain their normal acuity.

The most characteristic change is the inability to maintain that perfect co-ordination of muscular movement seen habitually in the working of the skeletal and ocular musculature, and called more especially into play in the pursuance of complex actions, such as those involved in the execution of technical movements, the harmonious working of the eyeballs, and in the maintenance of equilibration.

On the removal of one half of the organ there is an immediate loss of muscular co-ordination on the same side of the body. Let us suppose, for example, that the left half of the organ has been previously destroyed, it will be found that the animal (*e.g.*, dog) lies curled up with the concavity of the curve pointing to the side of the operation, while the muscles, and more especially those of the front limbs and neck, are rigid from muscular spasm. Tremulous movements may also be present, which become very greatly exaggerated on attempted movement (volitional spasm).

The pupils are rotated towards the opposite side, and there is generally some protrusion of the eyeballs. If the animal be lifted on to its feet, it promptly falls over towards the affected side, notwithstanding the marked abduction of the front limbs. If the attempts are violent the dog may roll over and over. There is also nystagmus in the homonymous eye. The head may be drawn somewhat backwards, or twisted to one side by the spasm of the neck muscles. After some time these phenomena pass away more or less completely, leaving only a certain amount of muscular weakness and, what is much more characteristic, muscular indecision, which may render the animal unable to withstand any

unexpected movement or to execute any sudden or unwonted act.

At the same time, it may be quite able to run about, or even to swim, in its ordinary way, while, as we have already mentioned, the intellect is perfectly normal.

Removal of the whole of the cerebellum necessarily affects the whole of the skeletal musculature, thus we get such marked rigidity of the neck and spinal muscles that opisthotonos is developed, while many of the other phenomena are correspondingly increased. On the other hand, the bilateral character of the affections renders them not so noticeable as in the former instance. The effects of the lesion take much longer to clear away, and Luciani has noticed that the dog very frequently recovers its power of swimming prior to that of walking or running. The tremors on attempted movement are generally very severe. The limbs, and more especially the anterior ones, are widely separated, so as to give the dog as broad a base for standing as possible.

The removal of the mesial lobe (or vermis) produces very similar symptoms, though in some instances we have, in addition, the development of curious retropulsive movements, by which an intended forward movement results in a backward one.

Division of the cerebellar peduncles.—A certain amount of very interesting information can also be obtained by noting the effects of section of the three peduncles which connects each half of the cerebellum with the cerebro-spinal axis. In every case the operation leads to the development of curious rolling movements round the long axis of the animal's body. At first the movement is from the sound to the injured side, though later the direction appears to be reversed. They are most evident after section of the middle peduncle, when Luciani states that they may be as frequent as fifty revolutions in the minute. There is also the marked rigidity or spasm and curvature of the body already described, while the head may be twisted so that the chin points away from the lesion, and the occiput is drawn violently backwards. There is also conjugate deviation of both eyes. Lussana has demonstrated that section of the contra-lateral peduncle arrests the rolling movements. Nystagmus is most marked after section of the middle and the inferior peduncles.

Connections of the cerebellum.—We have already seen that the chief connections of the cerebellum are through its peduncles with—

(1) The tegmental region of the crus, hypothalamus, and the

posterior part of the optic thalamus itself, thus bringing the organ into close touch with the great bundles of ascending or centripetal fibres coming from the periphery, and the ingoing axons of the great cranial nerves, such as the fifth and the eighth. At the same time, we must remember that the fibres of the antero-lateral ascending cerebellar tract of the spinal cord (fasciculus of Gowers) passes through the superior peduncle into the organ.

(2) The *nuclei pontis.*—These synapses bring the cerebellum into touch with the great descending cerebral projection systems, viz., the fronto-pontine, temporo-occipito-pontine, and the pyramidal.

(3) With the ingoing axons of the great sensory cranial nerves, and more especially those of the fifth and the vestibular branch of the auditory; many of the fibres of the latter sweep directly backwards to the cerebellar cortex, and thus convey impulses, which, as we will see later, play an extremely important part in cerebellar function.

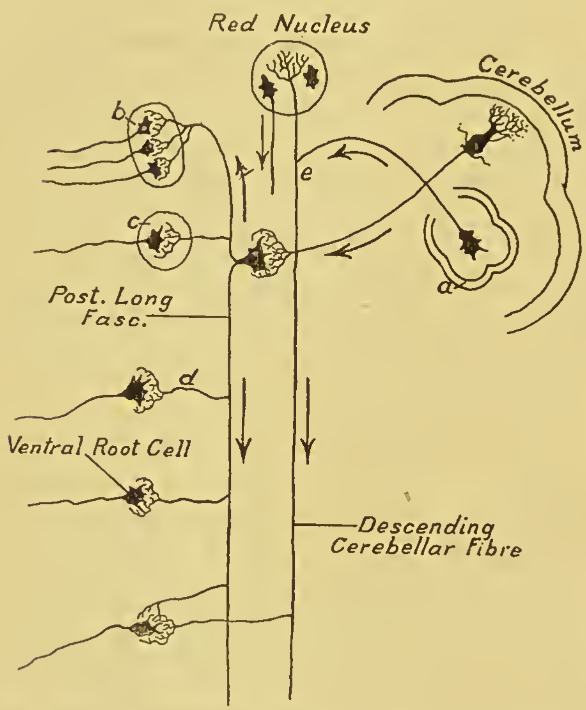

Fig. 451.—Scheme of the Connections of the Cerebellum with the Ocular Centres and the Ventral Spinal Cells.

There are also important bands of fibres linking the nuclei of Deiters and Betcherew with the organ, by which cerebellar influence can be conveyed, primarily to these nuclei, and later through the axons of Deiters' cells, lying in the superior longitudinal fasciculus and the vestibulo-spinal or descending cerebellar tract, with the motor cranial nuclei on the one hand and the motor root cells of the ventral cornua of the spinal cord on the other.

(4) With the postero-lateral ascending cerebellar tract of Flechsig in the spinal cord, thus forming another great sensory pathway by which centripetal impulses can reach the organ.

(5) With the olivary bodies in the medulla.

It will be obvious, therefore, that afferent impulses can reach the organ from all parts of the cerebro-spinal axis, and by a practically direct route from the semicircular canals, while, on the other hand, it can send efferent impulses to the cells of the cranial and motor nuclei and the anterior motor cells of the ventral cornua of the cord, thus probably controlling the tonus of the cells governing the ocular and skeletal muscles.

Lastly, the synapses with the descending projection fibres in the nuclei pontis and the tegmental region may influence largely the strength of the descending or ascending impulses coming from or going to the cerebro-cortical areas, and thus assist in the production of harmonious or co-ordinate muscular movements. Indeed, the activity of the motor neuron can be regulated or controlled by the cerebellum in three possible ways and situations:—(1) In the energising cells in the cerebral pre-Rolandic areas; (2) in the pons through the synapses of the nuclei pontis; (3) in the spinal cord, through the synapses of the fibres of the descending cerebellar or vestibulo-spinal fibres with the ventral motor cells.

Interference with any of the afferent pathways by which sensory impulses reach the organ induces to a greater or lesser extent loss of co-ordination. The various impulses can be grouped thus:—(1) Impulses coming from the terminals of muscular sensation in the muscles, &c.; (2) impulses coming from other sensory areas, such as the skin and the eyes; (3) impulses coming from the semicircular canals.

Muscular, tactile and visual sensations.—In locomotor ataxia, a chronic progressive disease of the spinal cord, chiefly located in the posterior columns (Goll and Burdach), a marked loss of co-ordination is perhaps the most characteristic symptom in the earlier stages of the condition. Thus if the patient be asked to close his eyes, thereby preventing the passage of sensory impulses to the cerebellum by that route, and to bring his feet together, so as to have a narrow base on which to support the body, swaying movements are at once set up, generally of such a violent character that the patient falls over if unsupported. The loss of equilibrium or ataxia is much worse if the ordinary cutaneous terminals of tactile sensation are also affected, as he is then unable to receive centripetal impulses through that avenue also. Very frequently the tactile sensation is markedly affected, so that the patient is unable to recognise the sensation of firm ground, and may imagine that he is walking on a bed of cotton wool, or a perfectly unstable element such as marshy soil or even cloud.

The close relations of these sensations to the maintenance of equilibration can be easily seen by watching such a patient performing his toilet, and impresses on the observer the significance of muscular sense and also, how, when one group of sensations is excluded others are instinctively and often successfully employed instead. Thus in washing his face the patient is careful to sponge only the one side of his face at one time, so that the other eye may remain open, otherwise he would probably fall forwards into the wash basin; or, if the muscular sensation of the arm be fairly intact, he will firmly seize the washstand with one hand while he washes his face with the other. In passing any clothing over his head, thus temporarily obstructing vision, he is forced to take special precautions to prevent accident, hence he usually sits down in an arm-chair before essaying the operation.

The great importance of visual impulses in the maintenance of equilibration is also well seen in locomotor ataxia, where they replace, with considerable success, the ordinary impressions coming from the muscles, skin, &c.

Any marked interference with the reception of visual impulses may also induce vertigo; thus when a person comes to the edge of a precipice, the sudden removal of the foreground frequently induces giddiness, &c.

Impulses from the semicircular canals.—These are undoubtedly the most important group of centripetal sensations concerned in cerebellar function. In disease of the canals (Ménière's disease) the principal symptoms are sudden and intense vertigo and vomiting. The structure of the canals has been already discussed in the section dealing with the Internal Ear, but it may be advisable to recapitulate here the points which have a direct bearing on the production of the centripetal impulses in the membranous labyrinth.

The canals are three in number on each side; they are in communication with the utricular division of the vestibule, and each has an enlargement or *ampulla* at one of its openings into the utricular cavity. The external canals lie in the horizontal plane; the superior canal of the one side lies vertically in a plane forming an angle of about 45° with the coronal plane, while the posterior canal is also vertical and lies in a plane parallel with the superior canal of the opposite side. From the accompanying diagrams it will be clearly seen that the two external canals are in the same plane, while the posterior vertical canal of the one side is in the same plane as the superior vertical canal of the other. It will be obvious, therefore, that the six canals are arranged in

three planes, each corresponding to the three different planes of space.

The non-ampullated extremities of the superior and posterior canals join, as shown in Fig. 362. There are, therefore, five openings from the membranous canals into the utricle.

Each ampulla exhibits on its inner surface a transverse ridge, the crista acustica, covered by epithelial cells bearing stiff hair-like processes. Somewhat similar elevations, the macula acusticæ, are found in the cavities of the saccule and the utricle. All these elevations receive fibres from the vestibular branch of the eighth nerve, the fibrillæ ending in arborisations around the bodies of the hair cells.

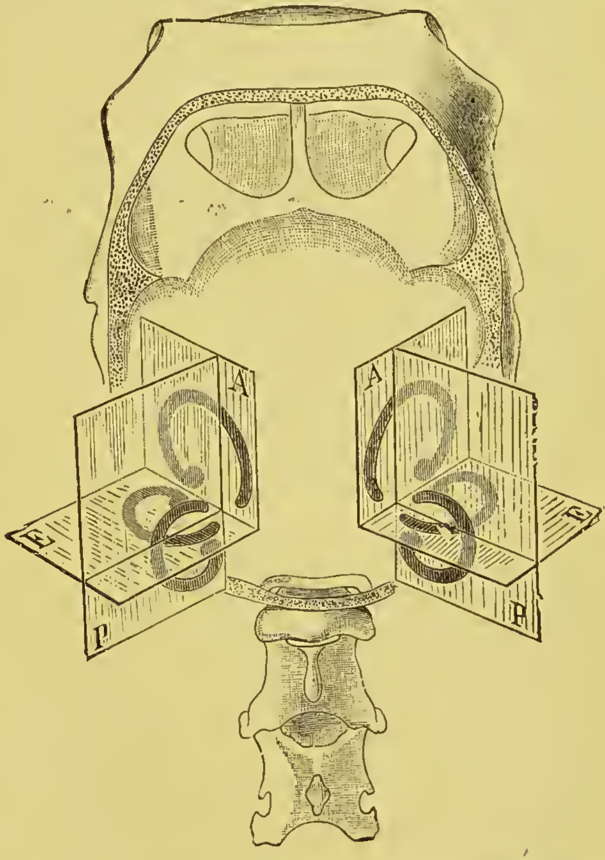

Fig. 452. — Diagram of the Three Semicircular Canals, showing their Positions in their Planes at Right Angles to One Another.

The external canals lie in the horizontal planes E; the superior vertical of the one side lies in the same plane as the posterior vertical of the other; A=anterior or superior; P=posterior.

The close relationship between the canals and equilibration can readily be demonstrated by noting the effects which follow the destruction of part or whole of the series of canals.

Flourens, the first experimenter to lay down definite evidence on this subject, pointed out that removal or injury of the canals in birds always induces a loss of equilibrium and the production of rotatory movements round an axis at right angles to the plane of the divided canal. The eyes twitch or roll violently, and irregular muscular movements appear, which may in some instances be so violent as to

prevent it remaining quiet even for a moment, or may indeed lead to serious injury.

The bird may execute somersaults, or it may spring suddenly into the air and come down on its occiput. In division of the horizontal canals the head swings violently from side to side, in pendular fashion, while after removal of the vertical ones the movement is in the antero-posterior plane, and may be so violent that the bird turns complete somersaults. The beak is not infrequently twisted to one side; indeed, in some instances the head may be turned so that the beak is pointing to the back of the neck.

If sufficient care be taken to prevent injury, either by padding the cage or by enveloping the bird in a soft cloth, the symptoms gradually pass away, so that after a lapse of from two to four weeks the bird may be able to sit quietly on its perch in the usual way. Even then, however, the equilibration is insufficient to enable it to withstand any sudden movement, such as a sudden jerk to the cage. The recovery is to be attributed very largely, if not entirely, to the excessive part now played in the co-ordinating mechanisms by vision, for if the bird be covered or hooded, or the eyes excised, all the inco-ordinative phenomena at once recur.

The method in which the terminations of the vestibular fibres are stimulated has been for many years a subject of great dispute. Whatever the exact cause may be, there can be little doubt that the hair-like processes, which are apparently intimately connected with the terminations of the nerves, are stimulated by variations in the tension of the fluids lying in the semicircular canals.

From the anatomical relations of the three semicircular canals to one another, and from their position in the three different planes of space, it will be apparent that movements of the head in any one plane will induce movements of the endolymph (and perilymph ?), so that we will obtain an increase of pressure in the one ampulla and a decrease in the corresponding one.

The stimulation occurs as the result of *variation* (acceleration or retardation) in velocity, and not from the actual position of the body or head. Thus if a person be firmly strapped down on a smoothly revolving table, it will be found that he experiences a sense of rotation on the inception of the movement, but after the rotation is perfectly uniform the sensation passes off; similarly, on retardation there is again a sensation of rotation, but this time in the reverse direction.

At the beginning of the rotation the head and the eyes are moved in a reverse direction to the movement of the table, but whenever the fluids become adjusted to the motion they pass back

to the normal position; conversely, as the table slows down, the head and eyes are rotated in the reverse direction, or, in other words, the movements of the head are identical with those of the endolymph.

Functions of the cerebrum.—The cerebrum is apparently the seat of all psychical function, for if the organ be destroyed there appears to be an absolute loss of all volitional, sensational and intellectual processes.

Again, in abnormal conditions where the cerebrum is either excessively small or diseased, the intellectual faculties are either very feeble, as in imbecility, or may undergo a steady decline.

The functional dependence of the lower parts of the cerebro-spinal axis on the cerebrum varies very greatly in the different classes of animals, thus if the volume of the pyramidal tracts in the cord be taken as an index of the extent of this connection, we find (v. Lenhossek) that, in the mouse, they form practically only 1 per cent. of the total volume of the cord, in the rabbit 5 per cent., in the cat 7 per cent., and in man nearly 12 per cent.

Consequently we should expect to find that decerebration in the higher apes would produce much more definite and pronounced effects than in the lower types.

Decerebration in birds. — The cardinal effects following the operation is the listlessness of the bird, so that it remains perfectly passive, unless stimulated, when it appears to wake up for a short time, and may execute all sorts of apparently rational movements, such as flying, walking, or even balancing itself on one leg.

As soon as the effects of the stimulus pass away, the bird relapses into its somnolent condition. One of the most striking effects produced is the total absence of all desire for food, though if grain be pushed into its mouth it may be reflexly swallowed.

After some time a certain amount of recovery takes place, so that the bird may walk about or even fly, but it never exhibits any tendency to hunt for or select any special food, nor does it show any evidence of fear on the approach of a hand, provided the movements are not too abrupt.

Decerebration in fish.—Removal of the brain in fish, such as the carp, does not seem to produce a complete loss of what we might call "higher" functions, for it is still able to swim about in the normal way, and to search for and seize its food. This is very well seen in the teleostei, where the fish may still be able to discriminate between various objects: thus if a number of

coloured wafers be thrown into the water, the fish will always select the red ones first. In the shark, however, the operation is followed by very characteristic results; it becomes perfectly passive and seems to have retained no volitional powers whatever. This may be ascribed to the destruction of the olfactory mechanism, which is the chief avenue in these fish by which centripetal impulses reach the cerebro-spinal axis.

Decerebration in the frog.—This is in many ways the most interesting example of this group of experiments, as the results are peculiarly distinct and the reflexes obtained after the operation are very easy to elicit.

The frog loses all voluntary power, so that it will remain perfectly passive for an indefinite period if left entirely alone; it makes no attempt to go in search of food, nor does it exhibit any signs of emotion such as fear. On the other hand, it responds perfectly and immediately to all forms of stimulation, thus if pinched it will jump; if placed in water, it will swim to the side of the vessel and even clamber up it; if stroked it will croak.

Many of the movements are of a distinctly purposive character, thus if the frog be placed on its back, it will turn round into its normal position, or if an obstacle be placed in its path it will either jump over or evade it. It must be realised, however, that these actions are entirely reflex and can only be elicited by appropriate stimuli, or that, in other words, they are perfectly involuntary in origin. Schröder has pointed out, however, that the results depend largely on the inclusion of the optic thalami in the operation. Thus if these ganglia are uninjured the frog may regain many of its apparently volitional powers, so that it may go in search of food, or even seek for a suitable place for hibernation.

Decerebration in the Dog.—The operation is difficult in the larger animals, chiefly from the hæmorrhage, which may be excessive, and from shock. Goltz, however, removed the whole of the cerebrum from a dog in three successive operations, and the results obtained were so well defined and characteristic that we will mention them in some detail. The animal lived for quite a long time after the operation (nearly two years) and recovered to such an extent that it was able to execute all sorts of movements; thus it could walk or even run in a somewhat lazy and purposeless fashion. The two most noticeable phenomena were the restlessness and the practically entire loss of the intellectual powers. Thus it seemed no longer to have any

memory, so that it did not evince either pleasure or annoyance at the approach of its master, though on being touched it tried to snap in a feeble and ineffective fashion. Similarly, there was a complete loss of sexual desire, curiosity, &c. It responded very slowly to calls, such as whistling, though it betrayed signs of fear when a pistol was fired in its immediate vicinity or a horn sounded. Any tricks which the animal was capable of performing previous to the operation were forgotten, and it could not be trained to learn fresh ones. The dog apparently saw objects, though it gave no indication that it was able to recognise them. Like the frog, it could evade obstacles and could select a pathway free from obstruction.

Grosglik obtained somewhat similar results after removal of both frontal lobes in the dog, namely, complete loss of memory, sexual desire, pleasure or annoyance, curiosity, &c., though the restlessness and irritability were, if anything, more marked.

From the results of decerebration, Goltz maintains that the cerebrum acts as an entity, or, in other words, that the whole of the cerebrum is concerned in the performance of the various psychical acts, such as thought, memory, sensation and volition.

The experiments of Fritsch and Hitzwig, Ferrier, and others, have, however, shown us that the cerebral cortex—more especially in the higher mammals—can be marked off into certain areas or districts which appear to be concerned with the performance of definite functions, such as the movements of groups of muscles, or the analysis of special sensations.

Cerebral localisation.—The functions of an area can be ascertained in several ways, as by noting the effects of stimulation or ablation, the so-called experimental methods; or by deductions derived from pathological data, such as hæmorrhage or tumour; or by ascertaining the histological connections of the area with the other parts of the cerebro-spinal axis, a method which has been amplified greatly during recent years by the histological methods of Golgi and Cajal, and the medullation method of Flechsig.

If it be carefully remembered that the cerebral cortex consists of cells which are in close functional connection, by means of collateral branchings and commissural fibres, with all other parts of the cortex, both in the same and the opposing hemisphere, as well as with the lower parts of the cerebro-spinal axis, it will be readily seen that the results of experimentation will be capable of many interpretations, and that any deductions the experimentalist may arrive at must be subject to the possibility of considerable fallacy.

Thus, even in the employment of certain phrases, such as motor area, the student is apt to imagine that the part has an automatic power of generating impulses which result in the production of muscular contraction, whereas, as we will see later, the cells are stimulated to activity by the reception of ingoing impulses from the periphery, as well as from other parts of the cerebral cortex which maintain them in a condition of tonus. The area might therefore be more logically called sensori-motor, and the acts themselves considered to be examples of very highly developed and augmented reflex action.

Excitation of the cortex.—*Methods.*—While different types of stimulation have been selected by the various observers, such as mechanical (Luciani), chemical (by the use of kreatin), the electrical may be justly considered to be the most satisfactory. Either the closing or opening shocks of a galvanic or a weak faradic current may be employed. The latter is generally preferred, the electrodes being either placed very closely together, or

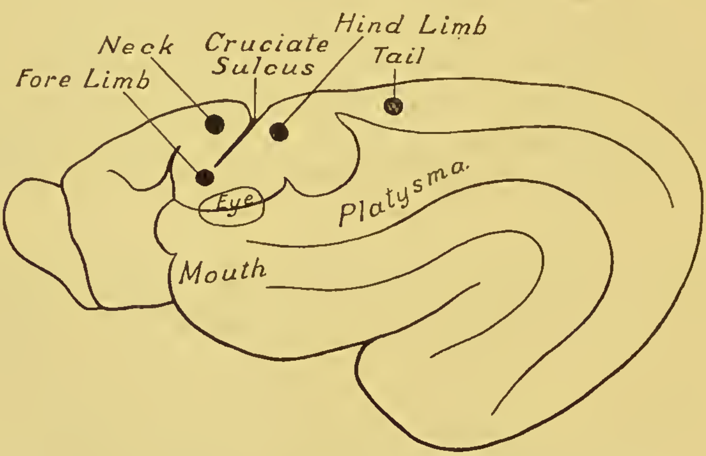

Fig. 453.—Diagram of Dog's Brain.

the one electrode may be placed over the selected part of the cortex and the other at some indifferent point. The stimulus should be as weak as possible, generally of an intensity just perceptible to the tongue. The method is necessarily open to a considerable amount of fallacy, especially if the stimulation be at all powerful, as it naturally tends to spread and thus to affect contiguous or physiologically connected areas. This objection may to a certain extent be obviated either by reducing the intensity

of the stimulation or by making a circular incision round the selected area, as far as the corona radiata.

The action of an anæsthetic on the cells may also impair very greatly their power of response to the excitation, so that we may obtain a feeble or even a negative result. The depth of the anæsthesia can, to a certain extent at least, be determined by the use of methylene blue. The temporary paresis induced by the action of the anæsthetic prevents the reduction of the pigment, so that the brain becomes tinted a light blue colour. On excitation, if the anæsthesia be not so deep as to prevent reaction, the ordinary reduction takes place and the part becomes colourless. The classical experiments of Fritsch and Hitzwig (1870) proved that excitation of certain parts of the cerebral cortex resulted in the production of definite localised movements on the opposite side of the animal's body. These areas were located more especially in the gyri immediately contiguous to the crucial sulcus. The experiments were extended later to the other lower animals, as the rabbit and cat, and even to the higher types, such as the apes.

Fig. 454.—Position of the Chief Cortical Areas in the Macacus (after Schäfer and Horsley).

It was found, also, that the large cortical areas could be subdivided into smaller ones which apparently controlled the muscles concerned in the execution of certain movements, such as abduction, adduction, flexion or extension at the various joints, the movements of the tail, eyes, &c.

The farther we pass up in the animal scale, however, the sharper becomes the localisation and the smaller the extent of the cortical area involved. Comparatively recent experiments by Sherrington and Gräunbaum on the brains of the orang, chimpanzee and gorilla show that in these highly developed apes the motor areas are still more localised, especially on the surface of the cortex, and that they are situated in front of the central or Rolandic

sulcus, instead of in the frontal and parietal lobes as in the macacus rhesus, and further, that they are arranged in a distinct relation to their order of emergence later, from the lower parts of the cerebro-spinal axis. Thus we have the area controlling the movements of the lower limb situated at the upper end of the fissure, then that for the arm, and finally, towards the lower part of the sulcus, areas controlling the musculature of the head and neck, face, lips, tongue, &c.

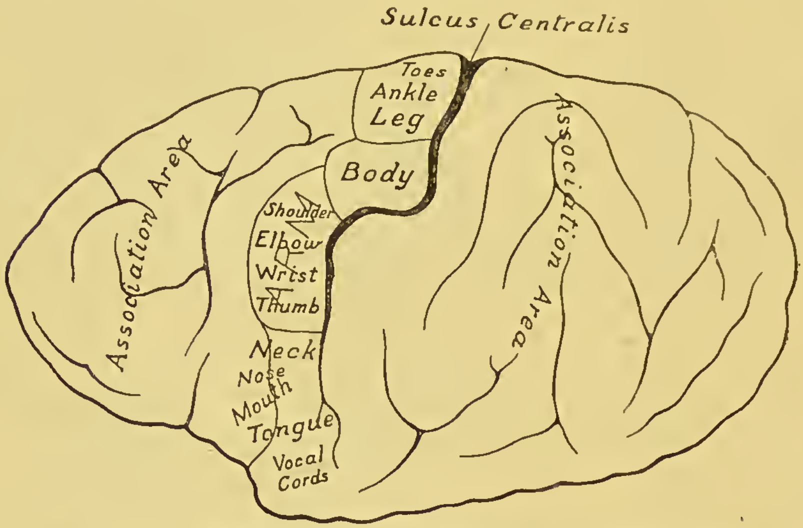

Fig. 455.—Diagram of Areas of the Chimpanzee's Brain (after Sherrington and Graünbaum).

The areas overlap to a very considerable extent, so that excitation towards the boundaries may induce movements in both the corresponding peripheral districts.

To prevent radiation of the stimulus to contiguous areas, a circular incision may be made around the selected part, and the electrodes then applied, when, if the stimulus be not too powerful, a contraction of the associated muscles of the opposite side of the body results. The connections of the cortical area with the lower parts of the cerebro-spinal axis can also be made out, either by actually removing or cauterising the part, or, as this interferes very seriously with the blood supply, by slipping a knife along between the grey matter and the corona radiata. The projection fibres, thus cut off from their trophic cells, undergo Wallerian degeneration, and thus we obtain a more or less distinct pathway which can be traced right down through the internal capsule, crus, pons and medulla into the pyramidal tracts of the cord as far as the

posterior horn of the grey matter, where, as we have already mentioned, the fibres end in synapses. The activity of the cells in these "motor" areas is maintained largely by the reception of ingoing or sensory impulses derived either from the periphery or from associated areas of the cortex: thus in the isolation experiment we have just mentioned, more or less complete loss of voluntary motor power takes place in the isolated portion. Again, Sherrington and Mott have demonstrated a somewhat similar effect after section of the ingoing nerves from a peripheral area, thus after division of the posterior nerve-roots of the brachial plexus there was a paralysis of the more intricate movements of the arm, so that the monkey was unable to raise its arm for climbing, or even to grasp firmly, though the muscles contracted readily enough when the corresponding motor areas were suitably stimulated. They also showed that the result was chiefly due to the loss of sensory impulses coming from the *skin*, for the paresis was not nearly so complete when the fibres coming from the muscles were divided. This affords very considerable support to the theory that the centres for skin sensation, such as tactile sense, lie in what are commonly called the motor areas. We might also deduce that the pyramidal cells of the cortex are maintained in working condition or tone by the ingoing impulses in exactly the same fashion as the anterior root cells in the ventral cornua of the spinal cord are by the impulses passing to them from the posterior root fibres (see Warrington's experiment, page 662).

Effects of powerful stimulation.—If the cortical excitation be severe, a series of movements of an epileptiform character appear, first of a tonic and later of clonic nature.

The convulsions appear first in the portion of the musculature supplied by the area, but later they spread over the rest of that limb, and then over the body as a whole.

From the histological arrangement of the cortex to the corona radiata we would expect that stimulation of the underlying white matter would produce similar effects to those following excitation of the corresponding part of the cortex. This is not the case, however. In the first place, excitation of the corona radiata does not produce the typical epileptiform convulsions we have just mentioned, the resulting muscular contractions being of a simple character, like those following stimulation of an ordinary nerve, the curve of contraction ceasing immediately after the excitation is stopped. Secondly, the reaction period (*i.e.*, the time which elapses between the excitation and

the appearance of the muscular contraction, is less in the case of the white matter, and, further, the duration does not vary to any great extent, whereas in the case of the cortex the delay may be increased by cerebral fatigue, or after the administration of drugs such as morphia, or in the anæsthesia of chloroform.

Again, cortical stimulation tends to produce effects of a particularly co-ordinate character, such as a movement at a joint; and further, these results may be modified by the entrance of some sensory impression, or by the presence of some psychical process. Tumours, also, pressing on the cortex, tend to produce epileptiform seizures similar to those obtained by powerful excitation of the grey matter. Finally, the electrical phenomena (demarcation currents) are far more pronounced on stimulation of the grey cortex than of the corona radiata.

A certain amount of very valuable evidence has also been obtained from pathological data, such as the growth of tumours in certain parts of the cerebrum, as well as from the irritation induced by the presence of splinters of bone and other foreign bodies, following fracture of the skull.

If the lesion be situated in the motor areas, the irritation may give rise to the development of a group of very characteristic symptoms, first described by Hughlings Jackson, and consequently called Jacksonian epilepsy. The attack is characterised by the appearance of muscular spasms, which are at first located in a definite area, but which tend to spread later to the other parts of the same limb, and may finally affect the whole musculature. The sequence in which the muscles are affected is peculiarly interesting, thus if the convulsive movements begin in the hand, they spread first up the arm, and later down the leg. This is due, apparently, to a radiation of the excitement from the primarily affected Rolandic area to those immediately contiguous. Unlike true epilepsy, consciousness is rarely lost, at least until the convulsions are very widespread.

In some positions, such as the antero-inferior part of the frontal lobes, stimulation may produce movements of the head and eyes; the movements differ in many respects, however, from those obtained on excitation of the pre-Rolandic areas, and it is possible that the results are chiefly of a reflex character. The response, for example, is very much more delayed, and the results are generally of a diffuse character. Again, stimulation of areas, which, as we will see later, are essentially concerned in the analysis of special sensation, such as the occipital lobes and the superior temporal, leads to the development of reflex movements

associated with sight in the one instance and with hearing in the other.

A very large part of the grey matter, however, does not seem to respond to stimulation, and is consequently called inexcitable.

While stimulation of a sensori-motor or kinæsthetic centre on the one side of the cerebrum generally induces movements of muscles on the opposite side of the body, this is by no means always the case; muscles which habitually act in concert, such as those of the mouth, larynx and eyes, can be thrown into activity by stimulation of the appropriate centres on the one side only. Sherrington has also pointed out that stimulation of the set of areas, as, for example, those governing the flexor muscles of the leg, is accompanied by an inhibition of the centres controlling the antagonistic group of muscles, or in this instance the extensors.

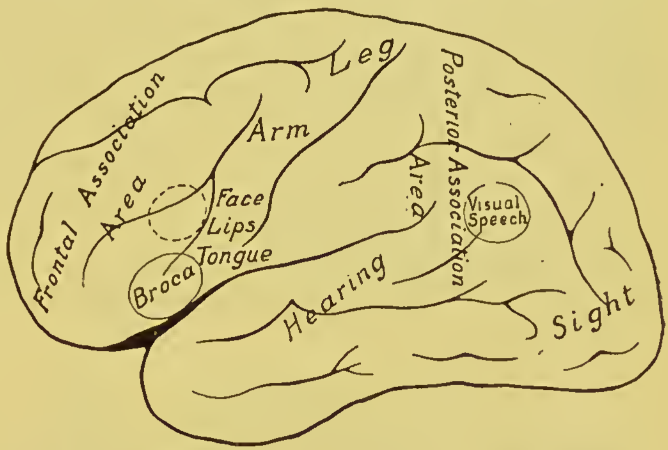

Fig. 456.—Probable Localisation of the Cerebral Areas in Man.

This is well shown in his experiment on the ocular muscles. He divided the third and fourth cranial nerves going to the left eyeball, so that the external rectus (supplied by the sixth nerve) was alone left active, and as a result obtained external strabismus of that eye. On stimulation of the cerebral centre there was not only a rotation of the unaffected or right eye towards the right, but also a movement of the left eyeball towards the mesial line, showing that the tonic contracture of the external rectus had been *reduced*, or, in other words, that the activity of the antagonistic centre had been diminished.

The size of the cortical areas bears no relation to the extent of the musculature they control, but depends chiefly on the complexity of the associated movements; thus the area for the arm is much larger than that for the leg, though the musculature of the latter is necessarily much the larger. Thus we have no distinct centres governing the movements of the muscles of the foot or of

the individual toes such as we find in the case of the hand, where there are separate centres for the thumb and the digits.

The subdivisions of the large cortical districts into the smaller centres is most marked in the case of the face, where we have definite areas controlling the movements of mastication, deglutition, the muscles of expression, &c.

Other results following excitation of the cortex.—Stimulation of the grey matter also induces a large number of other results, though it is difficult to say exactly whether they result from the excitation of separate centres. Thus we get, especially on stimulation of the motor areas, a rise in blood pressure due to a general vaso-constriction, especially if the excitation be not too powerful or prolonged, which may or may not be followed by a phase of vascular dilatation.

The heart is generally slowed, apparently from stimulation of the vagal centres, as the phenomenon does not appear if the vagi be previously divided. Stimulation of the frontal lobes very frequently promotes inspiration, though the researches of Spencer show that there are also centres affecting the other parts of the respiratory cycle.

Fig. 457.—Position of the Sensory Areas on the Outer Aspect of the Cerebrum (Flechsig).

There is also a close relation between the cortex and the performance of certain visceral acts, more especially micturition, and gastric and intestinal movement, and certain secretory acts such as the formation of the salivary and gastric fluids.

The sensory areas.

These are much more difficult to define with any degree of exactitude. This is partly due to the difficulty we have in inter-

preting the results of experiments, and also from the apparently wide cortical areas in which the fibres become distributed.

Flechsig has shown that the various fibres found in the cerebro-spinal axis acquire their medullary sheaths at different periods in fœtal life. The centripetal fibres going to the cerebrum and the cerebellum become medullated before birth, whereas, as a general rule, it may be said that the centrifugal and the association fibres develop theirs somewhat later. Thus if the brain of the newly born child be treated by Weigert's method it will be seen that the medullated portions are comparatively small, and located in fairly definite areas, such as the gyri surrounding the calcarine fissure in the hinder part of the brain (visual area), the gyri contiguous to the Rolandic fissure (sensori-motor or kinæsthetic area), and to a slight extent in the hippocampal convolutions (smell and taste) (Figs. 457 and 458).

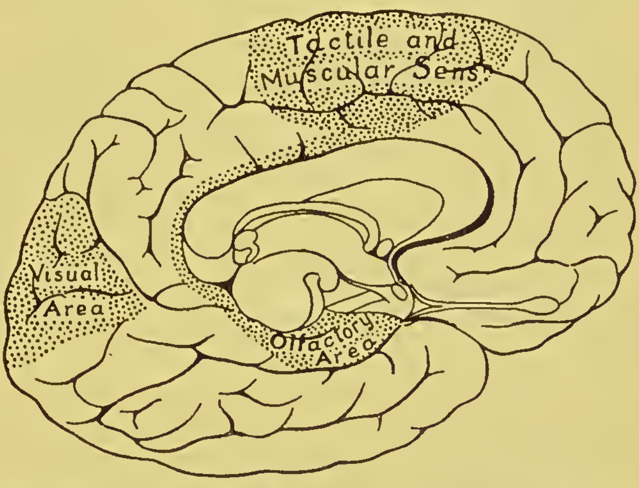

Fig. 458.—Position of the Sensory Areas on the Inner Aspect of the Cerebrum (Flechsig).

Immediately after birth the centrifugal fibres begin to undergo medullation, as special bands of fibres passing between the inexcitable areas of the grey matter, called by Flechsig the association centres, and also probably concerned in psychical functions.

He distinguishes three chief association areas, one situated in the frontal lobes, a second occupying the greater part of the parietal and temporo-sphenoidal lobes, and consequently called the parieto-temporal centre, and a small one in the island of Reil.

These large areas are connected to one another by association fibres and send comparatively few projection fibres down into the lower parts of the cerebro-spinal axis.

He has also shown that the fibres passing to the primary or sensory areas come chiefly from the lateral nucleus of the optic

thalamus, indeed, he distinguishes special bands of these fibres which medullate at slightly different periods. One set passes to the pre- and post-Rolandic convolutions (tactile and muscular sensation?) and the cuneate lobe (visual sensation) and others to the frontal lobes and the hippocampal gyri. These *cortico-petal* fibres apparently transmit ingoing impulses, and join the optic thalamus, which, as we have already seen, might be considered to be the terminal swollen end of the tegmental region where the chief sensory bands break up, with the cortical grey matter. He has also demonstrated the presence of cortico-fugal or efferent fibres passing away from these apparently sensory areas down to the basal ganglia; this would explain the reflex phenomena we have already mentioned which occurs on stimulation of the cortex, as, for example, the movement of the eyes and head on excitation of the occipital lobes and the pricking of the ears and attempts at vocalisation on stimulation of the upper temporo-sphenoidal lobe.

Ablation.—Portions of the grey cortex can either be directly destroyed by cauterisation or excision, or they may be washed away by a current of water as in Goltz's experiments.

Ablation is not entirely satisfactory as it interferes largely with the blood supply; it is better therefore to simply separate the cortex from the subjacent corona by slipping in a thin sharp knife and passing it along parallel to the surface, thereby dividing completely the connection, without actually removing any tissue or interfering to any great extent with the blood supply.

The **visual areas.**—The results of extirpation of the occipital lobe in the lower animals differ very considerably from those found in the apes, from the variation in the extent of the decussation and the arrangement of the fibres of the optic nerve. Again, in many of the lower animals the visual areas appear to be extremely diffuse. Some years ago Ferrier and Yeo showed that the removal of the angular gyrus was followed by complete blindness in the opposite eye, and that complete blindness followed the destruction of both the convolutions.

These results have not been confirmed by later observers; indeed, it has been shown that extirpation of the occipital lobes will produce blindness though the angular gyri are quite intact. A certain amount of recovery may however take place unless the adjacent parts of the temporal lobes be also removed (Schäfer).

The results of the lesion will be realised by a study of the accompanying diagram.

Where the lesion is situated at K, it will necessarily break the

pathway between the occipital cortex and the homonymous halves of the two retinæ, hence it will produce a similar field of blindness in the two eyes, or homonymous hemianopsia.

It has also been shown by Monk and others that certain parts of the occipital cortex are related to certain areas of the retinæ, thus the inner portions of the occipital lobes (inner surface of the cuneus) seem to be associated with the central zones of the retina (region of the maculæ lutæ); indeed, in the higher apes and in man, it is probable that this is by far the most important portion of the lobe. This view is also supported by Flechsig's observations, where the inner aspect of the cuneus, and more especially the grey matter in the immediate vicinity of the calcarine fissure, are the first parts to exhibit medullation. As already mentioned, removal of the one occipital lobe leads to half blindness in the corresponding halves of the two retina, but there is also a deviation of the head and eyes towards the opposite side, that is in the direction of the lost field of vision. Though pathological data support, on the whole, these observations, they rather incline us to the belief that there is a still greater differentiation of the occipital cortex into centres or cell groups, not only presiding over the analysis of both ordinary white and coloured sensation, but also concerned in the storage of visual sensations required later in the complex psychical processes underlying speech, &c.

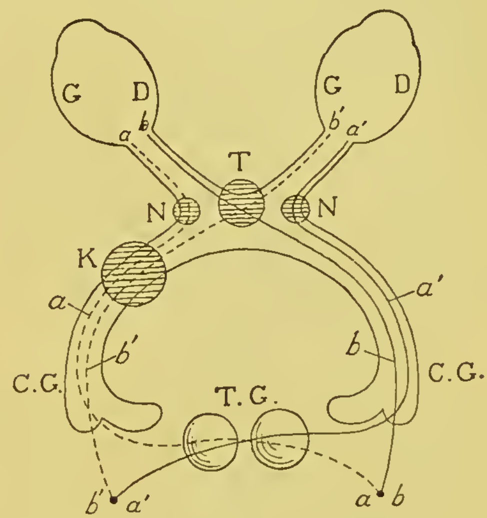

Fig. 459.—Diagram of Decussation of Optic Tracts.

T, Semi-decussation in chiasma; *T.G.*, fibres passing through the corpora quadrigemina; *aa′*, temporal fibres; *bb′*, nasal fibres; *C.G.*, corpora geniculata.

Olfactory sensation.—From histological, developmental and anatomical evidence there is considerable ground for the belief that the centres are chiefly situated near the anterior extremity of the hippocampal convolution (see Flechsig's diagram on the sensory areas (Figs. 458 and 459). Flechsig also maintains that the cortico-petal fibres pass to the grey matter not only the hippocampal convolution but also the whole extent of the gyrus

fornicatus, though the centres are undoubtedly in greater evidence in the vicinity of the uncus.

In animals where the sensation of smell is particularly well developed the uncinate gyrus is extremely large; indeed, in some instances it forms a pyriform lobule. Cajal has shown that many of the fibres of the olfactory nerve terminate directly in synapses in this area, and in the immediate vicinity, as, for example, the dentate gyrus.

The experimental evidence is rather contradictory. Ferrier and others have stated that movements of the lip and mouth, and others more or less closely associated with olfactory sensation, follow excitation of the hippocampal gyrus, and that removal of the area or its degeneration has been followed by interference with this sensation. On the other hand, Schäfer found no marked change in either smell or taste in monkeys after complete removal of the temporal lobes.

Auditory sensation.—The centres have been located by Ferrier in the upper temporal gyri, and, as we have already mentioned, Flechsig has demonstrated the development of medullated areas in this region at and shortly after birth.

Excitation produces reflex movements such as pricking of the ears, and further, Ferrier showed that ablation produces complete deafness. These results have, however, been denied by other observers. Clinical evidence supports on the whole Ferrier's arguments, and Donaldson and others have shown that there is probably a further subdivision, as in the visual area, for in lesions situated in the posterior parts of the upper two temporal convolutions there is generally word blindness (see "Aphasia").

Tactile and muscular sensation.—From the researches of Flechsig, and from the apparently close relation between the activity of the cells of the Rolandic area and ingoing impulses, as shown by the experiments of Mott and Sherrington (page 757), and the effects of making an isolating incision around the area, it would appear that these centres must be considered really sensori-motor in function, and further, that the sensations are chiefly those coming from the cutaneous and muscular sense organs. Again, in pathological conditions, such as cortical hæmorrhage, there is generally interference with both motor and sensory functions. Unfortunately there is a very wide divergence in the results obtained after ablation of the grey matter, thus while Munk, Mott and others have described the presence of both motor and sensory phenomena after ablation of the motor gyri, Schäfer

failed to obtain in many cases the slightest interference with tactile sensation. The sensation may be tested either by the application of an ordinary bull-dog clip or by simply stroking the skin, a method certainly subject to less chance of fallacy.

Speech.

This involves necessarily not only the energising centres which govern the muscles of the larynx or those of the hand (graphic speech), but also association areas in which the various impressions have been stored, and which are generally called the visual and auditory speech centres. The visual speech area is probably situated in the angular gyrus and the auditory in the upper part of the temporal lobes. The motor area for laryngeal speech is lodged generally in the lower inferior frontal convolution on the left hemisphere, and usually called Broca's convolution, while the motor area for graphic speech is probably situated almost immediately above. Lesions of any one part of this complex mechanism may induce aphasia, as the person may be unable to correlate the object under observation with any stored visual impression (word blindness) or sound (word deafness). In this case the failure lies in the sensorial part of the mechanism, and the condition is called sensory aphasia. On the contrary, he may be able to correlate the impression,

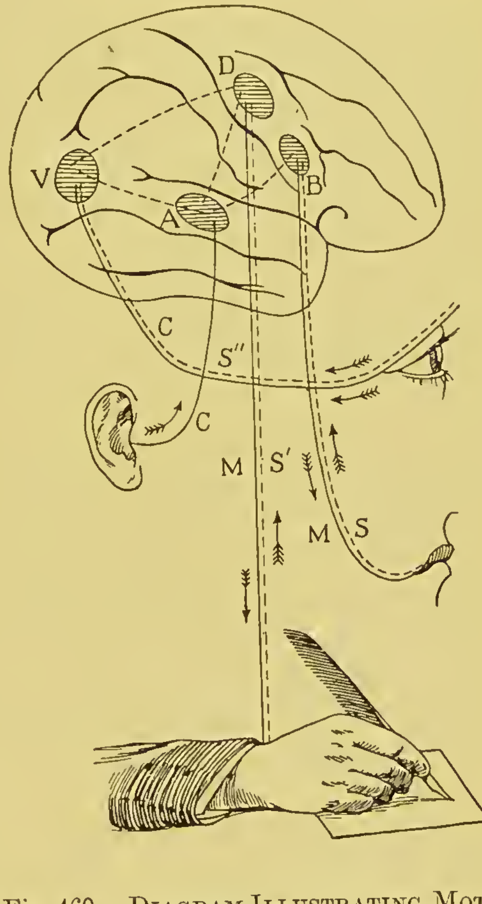

Fig. 460.—Diagram Illustrating Motor and Sensory Aphasia.

B, Broca's convolution (motor lip and tongue nerves); *D*, arm centre; *A*, word auditory centre; *V*, visual centre; *C*, centripetal fibres from eye and ear; *S*, *S'*, and *S''*, afferent fibres from articulation muscles of hand and orbit and lip; down lines between centres in cortex; association fibres between centres; *M*, *M'* centrifugal fibres from vocal centre (*V*) and unites expressive centre (*D*) to larynx and hand respectively.

visual or auditory, but may be unable to either speak it (laryngeal aphasia) or write it (graphic aphasia).

Special terms are often employed to express the different types, such as amnesia or interference with word or sound memories, and in motor aphasia, as aphemia and agraphia, to represent interference with Broca's and the word writing or cheiro-kinæsthetic centres respectively.

CHAPTER XVIII.

DEVELOPMENT.

THOUGH the development of the egg of the common fowl is generally taken as a typical example of the process, it must be remembered that it differs in many respects from that of the mammalian ovum. Thus, in the fowl, where the embryo develops in the shell after its extrusion from the parent, the egg is necessarily very large in size that it may contain a sufficiency of food material for the growth of the young tissues, whereas in the mammals, where the development takes place in the maternal uterus, the egg is very small and contains only a comparatively trifling quantity of yolk, all the food material necessary for the developmental process being drawn from the circulating fluids of the mother.

In the fowl, further, the division or segmentation process is limited to a small part of the ovum, called the germinal area (meroblastic segmentation), whereas in the mammal the whole of the ovum undergoes segmentation (holoblastic segmentation).

The ova also in their development require a supply of oxygen, which is obtained through the medium of a special vascular process —the allantois—which passes out from the hinder end of the embryo to the investing shell or chorion as the case may be, where the blood becomes oxygenated either directly through the shell or from the blood stream circulating through the sinuses in the maternal placenta.

The **Ovum.**—The ovum is a rounded cell invested in a distinct membrane called the zona pellucida, and measuring about 1·125 inch in diameter. The cellular protoplasm is laden with food granules and is called the vitellus or yolk. Near the centre of the cell is a rounded nucleus, the germinal vesicle, containing one or more nucleoli or germinal spots.

The germinal epithelium investing the ovary grows down into the cortex of the ovary, forming tubular processes (Pfluger's tubes), which later become cut off by fibrous tissue to form rounded masses of epithelial cells—the primitive Graafian follicles. Later one of

the cells of the follicle becomes greatly enlarged to form the ovum, while the remainder of the cells surround it, forming an investment of columnar cells which may be one or two rows deep. Somewhat later the follicle becomes distended with fluid (liquor folliculi) until rupture occurs, when the ovum escapes into the peritoneal cavity.

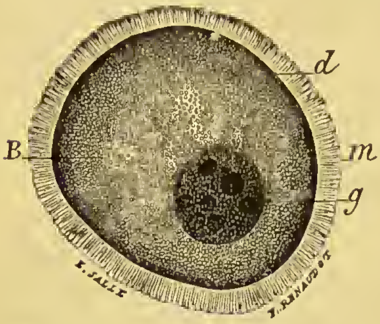

Fig. 461.—Ovum of Mouse.

m, Zona pellucida; *g*, germinal vesicle; *d*, cell protoplasm (yolk); *B*, attraction sphere.

By the action of the fimbriæ situated at the end of the Fallopian tube the ovum is drawn into the cavity of the duct and then passes by the action of the ciliated cells down to the uterine cavity. Fertilisation generally takes place in the cavity of the tube. After the escape of the ovum from the empty Graafian follicle, the cavity becomes filled with an accumulation of large yellowish cells called the luteal cells, probably derived by division of the epithelial cells lining the fibrous tunic of the follicle (zona glomerulosa). Bands of fibrous tissue pass in later among the cells, dividing them up into columns. In the non-pregnant condition, the cell mass or corpus luteum lasts for some ten or twelve weeks, when the cells begin to atrophy and finally disappear. In pregnancy, however, growth continues for several months, so that it may be nearly an inch in length, and of a bright yellow colour. After the eighth month it begins to shrivel and finally disappears, leaving a little puckered scar. It is generally supposed that the corpus luteum secretes an internal secretion which fixes the ovum to the uterine wall, and probably in other ways favours the continuance of the pregnancy. The presence of the ovary, indeed, seems to be of great importance in pregnancy, for removal of the ovaries generally terminates the pregnancy, though transplantation does not produce this effect.

Menstruation.—This phenomenon generally begins about the fourteenth year and extends until middle life, when the discharge becomes greatly reduced in amount and finally ceases. The discharge occurs generally at regular periods of twenty-eight to thirty days, and varies in quantity of from 100 to 200 grms. It consists of desquamated uterine mucous membrane with blood and mucus. It is doubtful how much of the uterine mucosa is actually removed at each menstrual epoch, but it is probable that the greater part is destroyed.

The relation of the menstrual to the ovulation process is

unknown. In many cases where there has been no history of previous menstruation pregnancy has occurred, and, similarly, fecundation may take place where menstruation is in abeyance, as during lactation.

On the other hand, there is no doubt that conception generally takes place in the fourteen days following the cessation of the menstrual epoch. In the lower animals sexual desire is only present during the period of œstrus or "rut," at all other times the female resisting the advances of the male.

In a large number of animals the œstral period occurs every four weeks—mare, monkey, &c.—in others every fortnight—sheep and sow—while in the dog it is generally from three to four months. There is a blood-stained mucous discharge from the vagina and considerable constitutional disturbance, with great nervous excitement of the animal. In women, on the other hand, sexual desire is most marked immediately after the cessation of the menstrual epoch.

It is probable that the function is governed largely by the condition of the ovary and by the action of an internal secretion formed in that organ.

Fertilisation.—As we have already mentioned (page 27), certain changes take place in the ovum previously to fertilisation, in which portions of the chromatin of the nucleus are expelled as the first and the second polar bodies.

Fertilisation is effected by the union of the head of the spermatozoon (the male pronucleus) with the remains of the original nucleus of the ovum (female

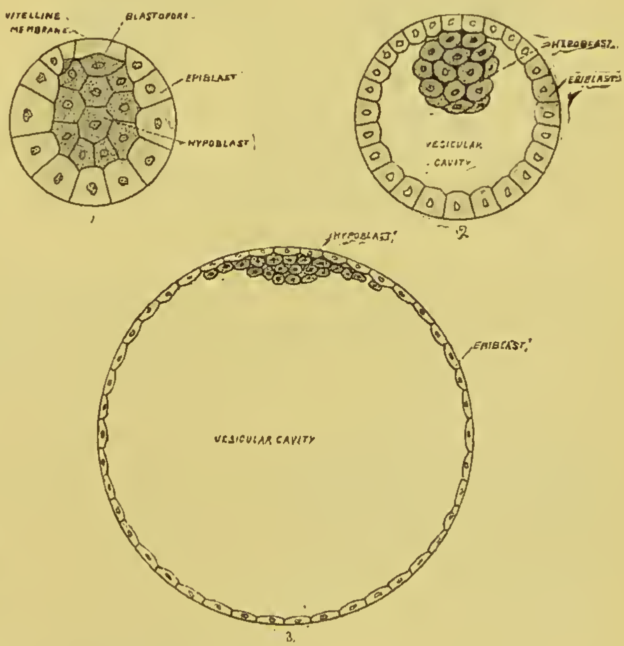

Fig. 462.—Three Early Stages in Development of Rabbit (after Van Beneden).

1, The metagastrula; 2, the commencement of the rapid enlargement of the egg; 3, the fully-formed blastocyst.

pro-nucleus). The head of the spermatozoon becomes separated from the body immediately after its passage through the zona pellucida.

The ovum is then passed on into the uterus, where it becomes imbedded in the fresh mucous membrane. While still in the Fallopian tube, however, the impregnated ovum undergoes the process of segmentation, to which we shall immediately refer. If fertilisation does not take place the ovum probably disintegrates after it reaches the uterus.

Segmentation.—The first change to take place is the cleavage of the nucleus and the yolk into two cells, of which one is larger and more transparent. These two cells continue to divide, until we get a mass of cells showing an outer and an inner layer, the former large and clear, and the latter small and dark (Fig. 462).

Fig. 463.—Three Consecutive Stages of the Blastoderm of a Chick in Early Stages of Incubation (after Koller).

1, Area opaca; 2, area pellucida; 3, blastopore. The blastopore is seen in the first to be crescentic, and is gradually converted by differential growth into a longitudinal groove, which closes to form the primitive groove.

After it reaches the uterine cavity there is a rapid increase in size from an accumulation of fluid, so that we get a vesicle invested by a layer of cubical cells and containing a fluid composed partly of water and partly of a solution of the foodstuffs contained in the yolk.

The inner group of dark cells is found at one part of the vesicle, attached to the outer layer of clear cells, forming a denser area called the embryonic area.

Formation of the Germinal Layers—Epiblast, Hypoblast, and Mesoblast.

The inner mass of dark cells in the germinal area is differentiated into two layers: of these, the outer blends with the original outer layer of clear cells, forming a single layer of cubico-columnar

cells—the epiblast; while the lower or inner layer becomes the hypoblast.

This constitutes the so-called bilaminar stage.

The embryonic area now becomes more pyriform in shape, and at its narrow end a streak, and later a groove, makes its appearance. This

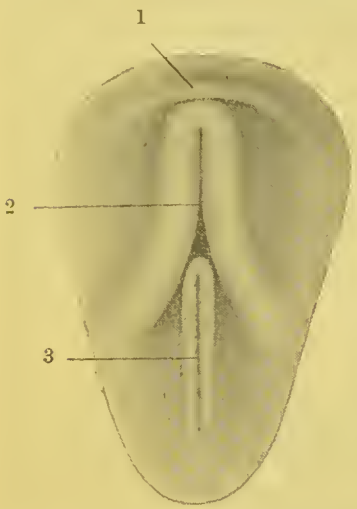

Fig. 464.—View of the Area Pellucida of a Chick's Blastoderm of about Eighteen Hours (after Balfour).

1, Amniotic head-fold; 2, neural groove; 3, primitive groove and streak.

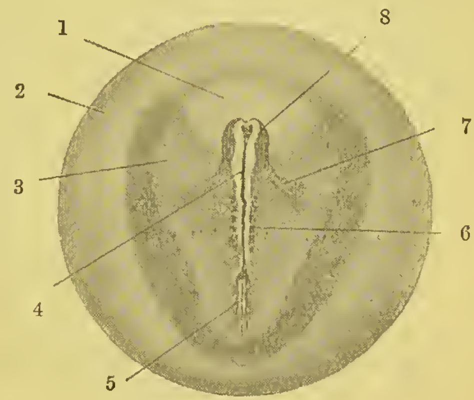

Fig. 465.—View of Chick's Blastoderm of about Twenty-four Hours (after Duval).

1, Pro-amnion; 2, area opaca; 3, mesoblastic lateral sheet; 4, neural groove; 5, primitive groove and streak; 6, protovertebræ; 7, vitelline vein; 8, head.

is due to a rapid division of cells, which later pass between the epiblast and the hypoblast, forming a third layer—the mesoblast (trilaminar stage) (Figs. 464, 465, 466).

In the area in front of the primitive groove two folds or ridges of epiblast rise up, called the neural or medullary folds, and enclosing a furrow—the neural groove. Ultimately the two folds coalesce so that the groove becomes a canal—the neural or medullary canal, which, as we shall see later, becomes narrowed down to form the canal of the central nervous system, while the epiblast of the medullary folds

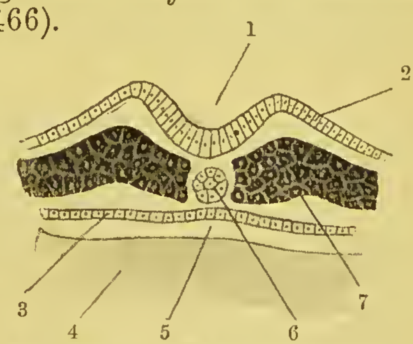

Fig. 466.—Cross-Section through a Blastoderm of about Twenty-four Hours.

1, Neural groove; 2, epiblast; 3, hypoblast; 4, yolk; 5, archenteron; 6, notochord; 7, mesoblast.

develops later into the nervous substance of the cerebro-spinal axis.

We have seen that the mesoblast is originally formed by the proliferation of the eells of the epiblast and the hypoblast situated at the primitive streak. By the development of the medullary groove and the notochord the plate of mesoblast beeomes broken up into two lateral portions, whieh, as we shall see presently, beeome further sub-divided. Immediately below the medullary eanal lies a solid mass of hypoblast—the notochord, whieh later forms a primitive supporting rod to the developing nervous system. The large mass of mesoblast situated at the side of the medullary eanal becomes divided up into squarish masses, the

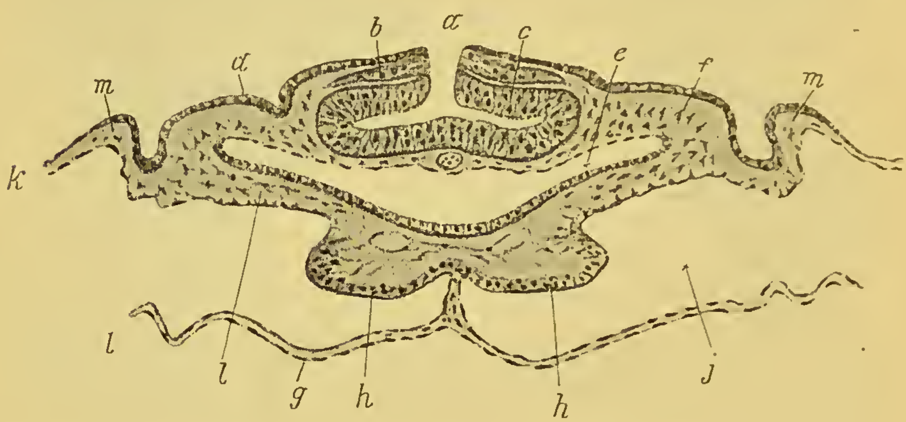

Fig. 467.—Transverse Section through Posterior Part of Head of Chick of Thirty Hours (×35).

a, Neural groove still patent; *b*, neural lamina of neural band; *c*, hind-brain; *d*, epiblast; *e*, cavity of alimentary canal (throat); *f*, mesoblast; *g*, hypoblast; *h*, invagination of mesoblast as before, the two tubes are here shown coalescing to form a single unimpaired one; *j*, pleuro-peritoneal cavity; *k*, somatopleure; *l*, splanchnopleure; *m*, commencing amniotic folds.

protovertebræ, whieh later form the bones and muscles of the vertebral column. The outer portion of the mesoblast splits into two layers, one immediately internal to the epiblast and ealled the somatopleure, and a seeond applied to the hypoblast—the splanehnopleure. Between the two layers lies a spaee—the eœlom or body eavity. This spaee is represented in the adult by the pleuroperitoneal eavity (Fig. 469).

Separation of the Embryo.—The whole of the embryo is formed from the embryonie area of the blastodermie vesicle, while the non-embryonie portion gives rise to an appendage corresponding to the yolk-sae in birds, the two parts become gradually

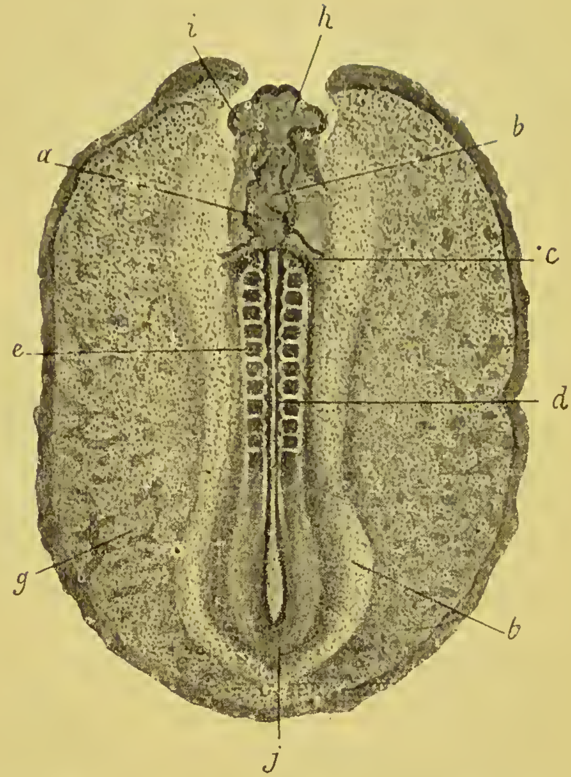

Fig. 468.—Chick (Forty-six Hours) seen from Below (× 15).

a and *b*, Heart; *c*, vitelline veins; *d*, neural tube (dorsal region); *e*, protovertebræ; *f*, area pellucida; *g*, area vasculosa; *h*, anterior cerebral vesicle; *i*, optic vesicle; *j*, tail.

separated from one another in the following way:—The embryonic portion becomes separated from the rest of the blastodermic vesicle by an ingrowth of the vesicular wall immediately below the developing embryo; the involution or folding is first seen at the anterior end, forming the head fold. A similar process also takes place posteriorly and laterally, so that the embryo becomes surrounded by a ditch, which, inclining inwards as it deepens, marks off the embryo from the yolk-sac. As the tucking-in process continues the sides of the embryo necessarily becomes bent in, so that we get a central space, connected below with the yolk-sac, and lined by hypoblast with its adherent layer of splanchnopleure. Beyond this lies the cœlom

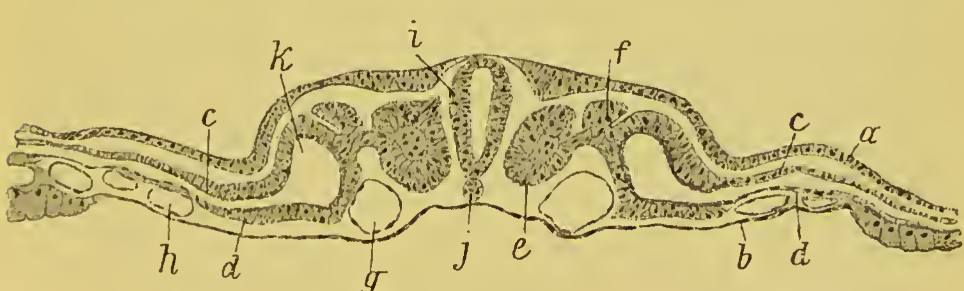

Fig. 469.—Transverse Section of Dorsal Region of Chick of Forty-five Hours (×50).

a, Epiblast; *b*, hypoblast; *c*, somatopleure; *d*, splanchnopleure; *e*, mesoblastic somite (or protovertebra); *f*, intermediate cell mass; *g*, aorta; *h*, blood-vessels of vascular area; *i*, neural column; *j*, notochord; *k*, cœlom.

or body cavity, bounded externally by the epiblast with its lining of somatopleure.

The connection of the central canal—or primitive alimentary canal—with the yolk-sac becomes gradually narrowed down to form a tubular and mesoblast process called the vitelline duct, and

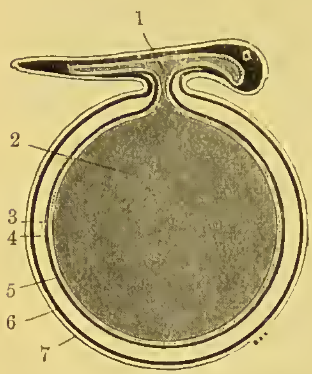

Fig. 470.—Evolution of the Fœtal Membranes of Skate.

1, Alimentary canal; 2, yolk in yolk-sac; 3, hypoblast of yolk-sac; 4, extra-embryonic cœlom; 5, mesoblast of yolk-sac; 6, mesoblast (serosa); 7, epiblast (serosa).

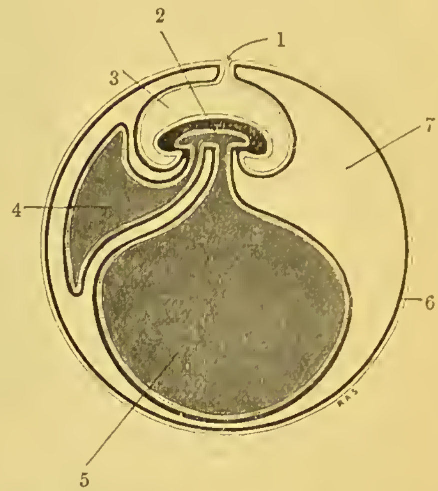

Fig. 471.—Evolution of the Fœtal Membranes in the Reptilia.

1, Amniotic canal; 2, embryo; 3, amniotic cavity; 4, allantois; 5, yolk-sac; 6, serosa; 7, extra-embryonic cœlom.

through it the hypoblast of the alimentary canal is continuous with those of the yolk-sac. These primary layers of the embryo give rise to tissues and organs differing markedly in function from one another.

Thus the hypoblast lining the primitive alimentary canal gives origin to the epithelium lining the various parts of the intestinal tract, and the glands developed from it, such as the liver, &c. The mesoblast gives origin, on the other hand, to the great supporting tissues of the body—bones, muscles, ligaments—also the circulatory system and the supporting framework of the great glands, while the epiblast gives rise to the whole of the nervous system, and the epidermal tissues, such as skin, hair, &c., and certain portions of the sense organs, such as the lens of the eye, &c.

The following table is from Minot :—

[Table

ECTODERMAL.	MESODERMAL.	ENTODERMAL.*
Skin (Epidermis).	1. *Mesothelium.*	Epithelium (of digestive tract).
Epidermal Structures.	Peritoneum.	Thyroid.
Hairs.	Pleura.	Thymus.
Nails.	Pericardium.	Tonsils.
Glands :—	Urogenital.	Trachea and Lungs.
Sebaceous.	Wolffian Body.	Œsophagus.
Sudorific.	Kidney.	Stomach.
Salivary.	Testes.	Liver.
Mammary.	Ovary.	Pancreas.
Corneal Epithelium.	Oviduct.	Intestine.
Lens of Eye.	Uterus.	Yolk-Sac.
Central Nervous System.	Vagina, &c.	Cæcum.
Ganglia.	Striated Muscle.	Vermix.
Nerves.		Colon.
Eye :—	2. *Mesenchyma.*	Rectum.
Optic Vesicle.	Connective Tissue.	Allantois :—
Optic Nerve.	Blood.	(Bladder).
Olfactory Organ.	Blood-Vessels.	Notochord.
Auditory Organ.	Lymphatics.	
Mouth Cavity :—	Spleen.	
Teeth.	Smooth Muscle.	
Hypophysis.	Fat Cells.	
Anus.	Marrow.	
Chorion :—	Skeleton.	
Placenta.		
Amnion.		

Fœtal Membranes.—The amnion is formed by upgrowths of the epiblast and the somatopleure given off immediately beyond the limiting folds. The folds pass upwards over the fœtus and finally coalesce, so that a tunic—the true amnion—is thus formed, covering the upper surface of the fœtus. After the folds have coalesced, a continuation of the layer becomes reflected around the inner aspect of the zona pellucida. This reflected portion is generally called the false amnion (Fig. 471).

The space between the fœtus and the true amnion is called the amniotic cavity and is filled with a fluid—the liquor amnii.

The allantois or second fœtal membrane is of very great importance as it plays an essential part in the transmission of food materials to the fœtus. As the umbilical vesicle in the mammalia

* Otherwise epiblast, mesoblast and hypoblast. By mesothelium Minot understands mesoblastic cells with an epithelial arrangement bounding the original pleuro-peritoneal fissure, and by mesenchyma cells of the nature of embryonic connective tissue thrown off from the mesothelium. That is, in short, "the whole of the mesoderm of the embryo except the mesothelial lining of the cœlom."

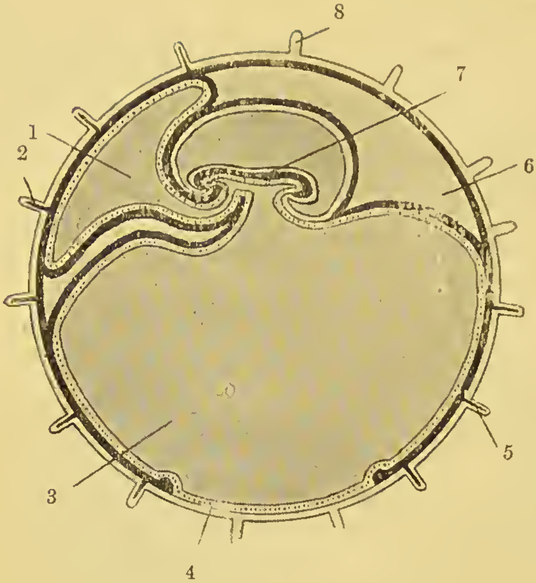

Fig. 472.—Diagram of the Fœtal Membranes of a Mammal.

1, Allantois; 2, allantoic villus; 3, fluid in yolk-sac; 4, prokalymma; 5, yolk-sac villus; 6, extra-embryonic cœlom; 7, embryo; 8, villus of serosa.

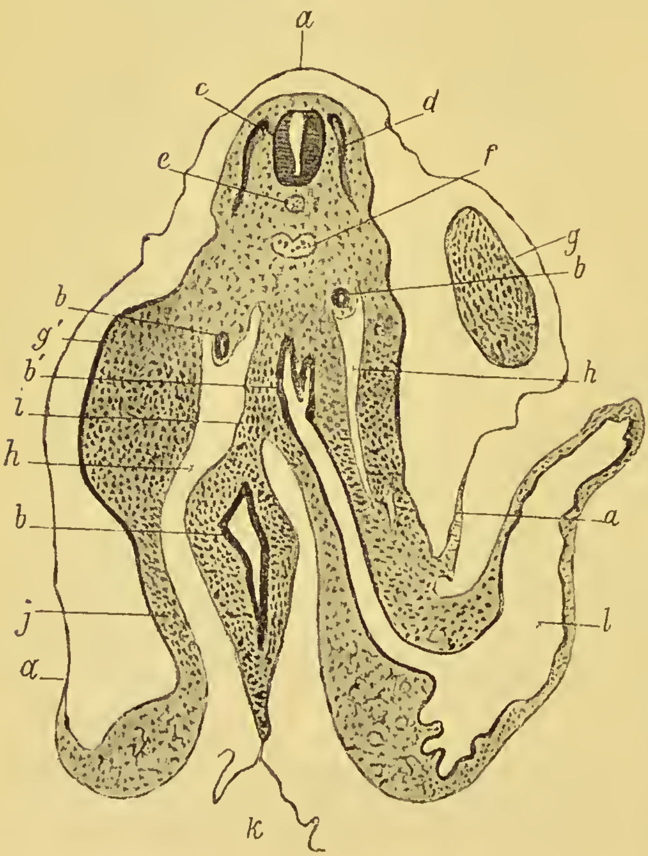

Fig. 473. — Transverse Section of Chick ($\times 35$), showing connection of Allantois with hinder end of Alimentary Canal.

a, True amnion; *b*, alimentary canal (hypoblastic lining of); *b′*, alimentary canal (hypoblastic lining of) receiving allantois; *c*, transverse section of spinal cord; *d*, muscle plate; *e*, notochord; *f*, aorta; *g*, transverse section of limb; *g′*, limb cut through before it separates from the body, hence section is not perfectly transverse, but to some extent oblique from side to side; *h*, pleuro-peritoneal cavity; *i*, splanchnopleure; *j*, somatopleure; *k*, shred of vitelline duct shown from obliquity of section; *l*, cavity of allantois communicating with alimentary canal, *b′*.

ceases at a very early date to be of any service as a source of food supply, it is clear that the embryo must at a correspondingly early date establish vascular connections with the parent, to ensure a food and oxygen supply and a method of escape for waste products. This is secured by means of the allantois, which forms both the umbilical cord and the fœtal part of the placenta. The allantois is developed from the posterior part of the primitive alimentary canal, as a hollow bud invested by a layer of mesoblast.

The lumen is of practically no importance; indeed, it may disappear entirely. The mesoblastic layer becomes rapidly vascularised and passed out in the space between the true and the false amnions to the opposing portion of the chorion which becomes the fœtal portion of the placenta.

The allantois contains two allantoic arteries derived from one of the terminal branches of the dorsal aorta of the embryo and a single allantoic vein.

From the true chorion, or that portion of the chorion to which the allantois has been applied, villi grow out into sinuses in the modified uterine mucous membrane. The majority of the villi are arborescent and contain an artery, vein, and capillaries, supported by connective tissue, the whole being invested by a fine layer of epithelium. The villi with the vascular spaces into which they project constitute the placenta.

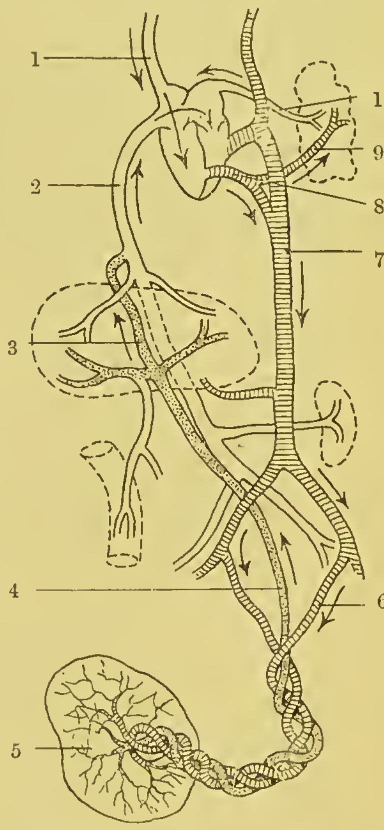

Fig. 474.—Scheme of the Fœtal Circulation.

1, Superior vena cava; 2, inferior vena cava; 3, ductus venosus; 4, umbilical vein; 5, placenta; 6, umbilical artery; 7, aorta; 8, ductus arteriosus; 9, pulmonary artery; 10, pulmonary vein coming from lung.

The **Fœtal Circulation.** — The blood coming from the placenta is carried up the umbilical vein to the liver, where the great bulk is passed into the ductus venosus and the inferior vena cava. It then reaches the right ventricle, whence it is directed through the foramen ovale into the cavity of the left auricle and ventricle and on to the aorta, and chiefly to the vessels supplying the head and

neck. From these areas the blood is returned by the superior vena cava to the right auricle and later the right ventricle and the pulmonary artery. As the lungs are functionless, the bulk of the blood is passed along a special fœtal vessel—the ductus arteriosus—to the thoracic aorta, where it mixes with that portion of the blood which has not passed up to the head and neck and passes to supply the lower parts of the body, a part being forced through the umbilical arteries to the placenta, there to be purified and oxygenated. It will be seen that the head and neck receive a purer supply of blood than any other part of the body. Immediately after birth the lungs distend and become functional, so that they require a large supply of blood, hence the ductus arteriosus is no longer required and consequently obliterates. The establishment of the pulmonary circulation also removes the necessity for the foramen ovale, so that it also disappears.

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